POSTPARTUM CONTRACEPTION PROVISION AND OPIOID USE DURING PREGNANCY

by
Leah Grambs Horton, MSPH

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Abstract

Background: Opioid use and opioid use disorder (OUD) during pregnancy are significant issues in the United States; yet little is known about postpartum contraception use among these women, particularly in comparison to women who do not use opioids. This study examined the relation between opioid use during pregnancy and postpartum prescription contraception.

Methods: Privately insured women with livebirths from 2011 to 2017 were identified using MarketScan, a database of paid health insurance claims. Provision of prescription contraception within 60 days postpartum was assessed among women who maintained continuous health insurance coverage through pregnancy and the first 60 days postpartum (n=1,291,352). A subset of women who used opioids during pregnancy were linked with infant records (n=63,897) to examine the impact of infant outcomes on contraceptive provision within 60 days postpartum. Contraceptive provision within 365 days postpartum was assessed among women with a livebirth from 2011 to 2016 and who maintained health insurance coverage through pregnancy and for any duration postpartum, up to 365 days (n=1,270,832). Multivariable logistic and multinomial regression models estimated the odds and relative risk ratio (RRR) of contraceptive provision by 60 days postpartum. Multivariable Cox Proportional Hazards models assessed the hazard of contraceptive provision within 365 days postpartum.

Results: Women with non-chronic and chronic prescription opioid use were more likely to receive postpartum prescription contraception than women with no opioid use; women with OUD were less likely to receive contraception. Women who used opioids had a higher RRR of sterilization verses no prescription method compared to women with no opioid use. Among women provided contraception, women with chronic prescription opioid use had the shortest time to provision and women with OUD had the longest time to provision. Increasing infant

hospital length of stay was associated with decreased provision of contraception by 60 days postpartum among women who used opioids.

Conclusions: Opioid use during pregnancy was associated with different levels of contraceptive provision overall and by method type across the postpartum period compared to women with no opioid use. This study highlights the need to address disparities in postpartum contraceptive provision among women who use opioids, particularly for women with OUD.

Advisor: Donna Strobino, PhD

Committee of Thesis Readers

Committee Members	Department
Emma Beth McGinty, PhD, MS Associate Professor	Health Policy and Management
Donna Strobino, PhD Professor and Thesis Advisor	Population, Family, and Reproductive Health
Caroline Moreau, MD Associate Professor	Population, Family, and Reproductive Health
John McGready, PhD Senior Scientist	Biostatistics
Pamela K. Donohue, ScD, MS Associate Professor	Johns Hopkins School of Medicine

Alternate Committee Members

Ramin Mojtabai, MD Professor	Mental Health
Alison Gemmill, PhD, MPH, MA Assistant Professor	Population, Family, and Reproductive Health

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Chapter 1. Introduction and Specific Aims

1.1 Introduction

Over the past 60 years, expanded contraception access and use has contributed to gains in women's health, the health of families, and the social and economic opportunities available to women in the United States (US) [1, 2]. Contraception use in the postpartum period, defined as the first year following delivery, is an important aspect of women's health and confers many of the same benefits of contraception use generally, with the added advantage of allowing women time to recover from pregnancy and childbirth and focus on caring for their newborn. Postpartum contraception use in the US has remained steady over the past decade, with increases in uptake of highly effective methods, such as the IUD, among women who use postpartum contraception [3-5].

Postpartum contraception use among marginalized groups of women, including women who misuse opioids or have opioid use disorder (OUD), is a topic of increasing focus because women with OUD represent a growing segment of the population and face additional clinical and social risks [6]. While research on postpartum contraceptive use has focused on identifying disparities by race/ethnicity, income-level, and among teen mothers, there is more limited work about use and potential disparities among women who use opioids during pregnancy [7-10]. Understanding the patterns, correlates, and predictors of contraception use among women who use opioids during pregnancy is a crucial gap in the literature addressed by this research.

The misuse of opioids and opioid use disorder among women of reproductive age is a significant public health concern. Pooled national survey data from 2005-2014 indicate that 1.4 million women of reproductive age and over 50,000 pregnant women have misused prescription opioids in the past 30 days [11]. The prevalence of maternal opioid abuse at the time of delivery

has increased from 1.5 cases per 1,000 hospital deliveries in 1999 to 6.5 in 2014 [12]. The growing misuse of opioids among this population has significant implications for maternal and infant health. Between 2007 and 2016, the percentage of pregnancy-related deaths in the US involving opioids doubled, increasing from 4% to 10% [13]. Additionally, there is growing evidence that opioid use and OUD is a significant contributor to increasing rates of severe maternal morbidity [14]. Women who use opioids during pregnancy are more likely to experience postpartum hospital readmissions and have a higher obstetric comorbidity index at the time of delivery [15]. In tandem with rising rates of opioid use during pregnancy, the incidence of neonatal abstinence syndrome (NAS), the most common sequela associated with fetal exposure to opioids, increased 300% from 1.5 cases per 1,000 hospitals births in 1999 to 6.0 in 2013 [16]. Increasing access to and provision of postpartum contraception is one strategy to help minimize these adverse outcomes as it may help women who misuse opioids avoid unintended pregnancies, delay mistimed births, and focus on their own health.

Despite being a crucial component of reproductive health, postpartum contraception use in women with OUD is not well understood. With an estimated 85% of pregnancies to women with OUD being unintended coupled with an increasing number of pregnancies impacted by opioid use in the US, identifying the prevalence and use patterns of postpartum contraception among women with OUD is imperative for preventing unintended pregnancies and improving reproductive health outcomes in this population [12, 17-19]. Prior research examining postpartum contraception use among women who use opioids has largely focused on women insured through Medicaid or select groups actively enrolled in drug treatment programs or clinical trials [20-26]. To our knowledge, the current research is the first to examine postpartum contraception among women who use opioids in a commercially insured population. This

dissertation research explored the relation of opioid use during pregnancy with postpartum contraceptive provision, comparing women who did and did not use opioids during pregnancy at multiple time points during the postpartum period.

The three specific research aims of this dissertation were to:

Aim 1: Evaluate the association between opioid use during pregnancy and prescription contraception provision by 60 days postpartum, including by contraceptive method type.

Aim 2: Evaluate the time to first prescription contraception provision during the postpartum period for women who did and did not use opioids during pregnancy, including by type of opioid.

Aim 3: Assess if adverse newborn outcomes are associated with provision of prescription contraception within 60 days postpartum among women who used opioids during pregnancy.

These research aims were evaluated using a nationwide database of paid health insurance and pharmaceutical claims from privately insured patients in the US from 2010-2017. This database allowed for the identification of opioid use during pregnancy and the analysis of postpartum prescription contraception provision for as long women maintained continuous health insurance coverage. Analyses for Aims 1 and 2 were adjusted for maternal age at delivery, year of delivery, characteristics of the geographic location in which women resided, health insurance plan type, several comorbidities, non-opioid substance use, mode of delivery, and, for Aim 1, whether a postpartum health visit occurred within the first 60 days postpartum. Analyses for Aim 3 were adjusted for the same covariates as well as several infant variables. The measures of postpartum contraception used in this research are clinical performance measures recently

endorsed by the National Quality Forum, ensuring that results of this research are in accordance with nationally recommended measures [27].

This research addresses a significant gap related to the health of women of reproductive age who use opioids. The postpartum period offers a window of opportunity to increase uptake of moderately and highly effective forms of contraception among women who desire to use postpartum contraception because they are in close contact with the healthcare system and are motivated to prevent unintended pregnancy [28-30]. The results of this research help elucidate patterns of postpartum contraceptive provision among women who use opioids during pregnancy and how these patterns compare to women who do not use opioids among a sample of privately insured women who are not often the focus of substance use or contraceptive research. Furthermore, this research serves as a valuable resource for clinicians who work with opioid-using patients, particularly in terms of counseling and educating patients on their contraceptive options. Postpartum contraception plays a crucial role in women's health and is of particular importance among women with OUD, who have very high levels of unintended pregnancy and face significant social and clinical challenges.

1.2 Dissertation Overview

This dissertation is organized into five chapters. The first chapter provides an introduction to the study and overview of the research aims. Chapter two presents a comprehensive literature review covering the topics of contraception use generally, postpartum contraception, opioid use during pregnancy, and reproductive health outcomes among women with substance use disorders. The literature review informs the conceptual framework underpinning this research, which also is presented in Chapter two. Chapter three describes in-depth, the study design, data source, study sample, and analytic methods used in this research.

The results of the analysis, including descriptive statistics, univariate, bivariate, and multivariable analyses results, along with several sensitivity analyses, are presented in Chapter four. The final chapter, Chapter five, provides a discussion of the study findings, reviews the study strengths and limitations, public health implications of the study result, and the study conclusion.

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Chapter 2. Background and Conceptual Framework

2.1 Overview

This chapter presents a literature review on contraception use, including during the postpartum period, opioid use in women and during pregnancy, and contraception use among women with substance use disorders or who use substances. The significance and rationale for this study are presented next within the context of limitations of prior research. The chapter concludes with a review of the conceptual framework that served as a guide for this research.

2.2 Contraception and Women's Health

The benefits of contraception for the health and well-being of women are widely recognized. Contraception allows women and their partners to plan, delay, and space pregnancies over their reproductive lifespan. It also helps prevent unintended pregnancies, avert maternal deaths, and expand women's economic, social, and educational opportunities [1, 2].

Since the introduction of the combined-hormonal contraceptive pill in 1960, the use of contraception has become universal in the United States with 99% of women aged 15-44 reporting any lifetime use of contraception [3]. The prevention of unintended pregnancies and birth spacing are two direct benefits of contraception use and expanded contraception use in the US has resulted in substantial declines in rates of unintended pregnancy and abortion [4, 5]. This decline is important for women's and infants' health as unintended pregnancies are associated with lower levels of prenatal care, low birth weight, and increased risk of maternal depression or depressive symptoms [6-9]. In the US, unintended pregnancies are increasingly concentrated among women with low education, low income, and women of color [10]. Contraception also reduces pregnancy-related morbidity and mortality by reducing a woman's exposure to pregnancy [1]. The health risks associated with pregnancy, including exacerbation of existing illnesses, gestational diabetes, gestational hypertension and preeclampsia, significantly exceed

the risks associated with contraception use [11]. There are also non-contraceptive health benefits of hormonal contraception use including treatment for menstrual cramps, heavy menstrual bleeding, migraines associated with the menstrual cycle, and acne [12].

The benefits of contraception and family planning extend beyond physical health. Contraception allows women to expand their role in society through increased employment outside the home, pursuit of higher education, and economic independence. There is strong evidence linking expanded contraception use and associated delayed childbearing to gains in female education, particularly at the college level and beyond [13-16]. Similarly, studies have demonstrated an empirical link between the introduction of the pill and an increase in female participation in the work force [17, 18]. Expanded contraception use has significantly contributed to women's increasing earning capability, and by delaying childbearing, women can enter parenthood with more economic stability [13, 19] [20-23]. Delayed childbearing has important ramifications for the health and well-being of women and their offspring. Entering parenthood as a teenager or as a result of an unplanned pregnancy is associated with increased depressive symptoms and anxiety among mothers and poorer parent-child relationships, which may be due in part to the reduced economic stability that is often present among teen parents [24-26].

Table 2.1 FDA Approved Contraceptive Methods Covered by the ACA Contraceptive Mandate

Contraceptive Method
Surgical Sterilization
Implant Sterilization
Implantable Rod
IUD-Copper, progestin
Injection (DMPA)
Oral Contraceptive Pill – combined, progestin-only, extended use
Patch
Vaginal Ring
Diaphragm with Spermicide
Sponge with Spermicide
Female Condom
Spermicide alone
Emergency Contraception- progestin, ulipristal acetate

The extensive evidence supporting the benefits of contraception is the reason why in 2011, the Institute of Medicine recommended that all FDA-approved contraceptive methods be considered preventative health care for women (Table 2.1)

[27]. This recommendation is the basis for the Affordable Care Act's (ACA) "contraceptive mandate", which requires that women have access to the full range of FDA-approved contraceptive methods with no cost-sharing or copays from their health insurer [28]. Since the introduction of the contraceptive mandate, out-of-pocket costs for contraception for insured women have decreased substantially and the percentage of women using long-acting reversable contraception, such as the IUD and implant, has increased [28, 29].

2.3 Postpartum Contraception in the United States

Postpartum contraception refers to contraception used in the first 12 months following pregnancy and includes all available contraceptive methods, ranging from sterilization to the lactational amenorrhea method [30]. The use of postpartum contraception helps prevent rapid repeat pregnancies, defined as pregnancy within 18 months after a live birth, and unintended pregnancies, resulting in better health outcomes for women, their infants, and families [31, 32]. The result of a recent systematic review in high-resource country settings indicated that interpregnancy intervals shorter than six months may be associated with increased risk of preterm birth and infant death [33]. The importance of the postpartum period as a window of opportunity to counsel and provide women with a contraceptive method of their choice has been increasingly recognized as women are motivated to prevent pregnancy and have frequent contact with the healthcare system during this period [34].

Measures of postpartum contraception vary depending on the data source and research question, making comparisons difficult across studies and data sources. In 2016, the US-based National Quality Forum (NQF), a non-profit, nonpartisan organization, endorsed two clinical performance measures for assessing the quality of postpartum contraceptive care [35]. The first measure addresses the receipt of a moderately or most effective contraceptive method by three

and 60 days postpartum [35]. Moderately effective contraceptive methods include depot medroxyprogesterone injection (DMPA), the pill, patch, ring, or diaphragm and the most effective methods are sterilization, the IUD, and implants. The second measure is focused on long-acting reversible methods (LARC), which includes the IUD and implants, measured at three and 60 days following delivery [35].

The timeframes of three and 60 days represent clinically significant time points during the postpartum period. Measuring the provision of contraception within three days of delivery corresponds to the immediate postpartum period when many women are still hospitalized following delivery. This time is optimal to provide postpartum contraception, particularly LARCs, as it is both safe and convenient to do so then [36]. There are several reasons why immediate postpartum contraceptive provision is beneficial. Foremost, immediate provision eliminates the need for an additional visit(s) to a healthcare provider to obtain contraception. Research findings demonstrate that women at the highest risk for unintended pregnancy in the postpartum period also have low postpartum visit attendance, which includes women with substance use disorders (SUD) [37, 38]. Secondly, 40-57% of women report the resumption of sexual intercourse prior to their 6-week postpartum visit, putting them at risk for pregnancy [39, 40]. Finally, randomized trials have demonstrated that immediate postpartum LARC insertion results in greater adherence to the method and decreases the risk of pregnancy when compared to delayed insertion of postpartum LARC [41]. The 60-day timeframe represents the clinically recommended timeframe by which women should receive contraceptive care, typically at the six-week postpartum care visit [35]. The new NQF evidence-based measures enhance continuity across studies and are designed with feasibility and usability in mind.

Estimates of the postpartum contraceptive prevalence rate are quite variable in the US. National estimates from the Pregnancy Risk Assessment Monitoring System (PRAMS) indicate that approximately 80% of women queried postpartum report used some form of contraception in the first four months following delivery [42]. Data from the National Survey of Family Growth (NSFG) indicate that 72% of women use some form of contraception within three months following delivery [43]. The most commonly reported methods were moderately effective methods, such as the pill, patch, or ring, and less effective methods including male condoms, withdrawal, and the rhythm method [43]. Approximately 25% of women, however, reported using no method and this proportion remained consistent throughout the postpartum period [43]. The results of a study using data from women and families enrolled in the Military Health System noted that 36.7% of women did not initiate any prescription form of contraception in the first six months following delivery [44]. Among women who did initiate prescription contraception, 7.0% relied on tubal ligation or partner vasectomy; 16.9% initiated an IUD or implant; 2.5% were prescribed DMPA; and 36.8% were prescribed a pill, patch or contraceptive ring [44].

Estimates of postpartum contraception use are available specifically for the privately insured population; however, these estimates are limited to prescription contraceptive methods which include female sterilization, the IUD, implant, DMPA, the pill, patch, ring, and diaphragm [45]. Law, et al. employed the recently endorsed NQF measures to assess postpartum contraception use at three and 60 days postpartum in the MarketScan database, the source of data for this research. Between 2005 and 2014, the percentage of women using a moderately or most effective method of contraception within 60 days postpartum increased from 24.1% to 38.6% among women 15-20 years old and from 32.5% to 37.7% among women 21-44 years old [45].

The pill was the most commonly used form of prescription contraception at 60 days postpartum among both age groups and in every year across the study time period [45]. At three days postpartum, which serves as an indicator for the immediate postpartum period, the percentage of women receiving a moderately or most effective method, however, decreased over the study time period. For 15-20-year-old women the percentage decreased from 6.0% in 2010 to 3.2% in 2014 and from 10.4% to 8.0% among women aged 21-44 [45]. For both age groups, female sterilization was the most common form of contraception in the immediate postpartum period and immediate postpartum LARC was rare (<0.2%).

Several recent studies have examined the circumstances and characteristics associated with receipt of postpartum contraception in the US. The results of a nationwide retrospective cohort study examining receipt of immediate postpartum LARC and sterilization prior to discharge for a hospital delivery showed that receipt of LARC increased significantly from 1.86 per 10,000 hospital deliveries in 2008 to 13.5 in 2013, while sterilization rates remained steady over the same time period [46]. In adjusted models, women with non-private insurance, which includes Medicaid, Medicare, self-pay, or no charge, were five times more likely to receive immediate-postpartum LARC than privately insured women (aOR: 5.23, 95% CI: 3.82-7.16). Women with non-private insurance were also more likely to be sterilized than privately insured women (aOR: 1.90, 95% CI: 1.38-2.63) [46]. Other characteristics significantly associated with immediate postpartum LARC receipt included delivering at an urban teaching hospital and in the later years of the study period and having a medical comorbidity [46]. Women in the Southern region of the US were significantly less likely to receive LARC and significantly more likely to be sterilized compared with women in the Western region (reference region) [46].

A second, smaller study examined postpartum LARC receipt at 90 days postpartum among women delivering at a single urban teaching hospital in Ohio [47]. Receipt of LARC by 90 days postpartum among women in this sample was significantly associated with adequate prenatal care but was not associated with insurance type in adjusted models [47]. A final study based on PRAMS data from 2012-2015 explored factors associated with postpartum LARC use [48]. The overall prevalence of LARC was 15.3%, with significant variation by state [48]. Among women using reversible contraception, the prevalence of LARC was highest in Alaska (37.6%) and lowest in New Jersey (11.2%), with a general trend of higher LARC prevalence in the Western US [48]. Women who reported using LARC were significantly more likely to be younger, be publicly insured, report their most recent pregnancy as unintended, and report attending a postpartum check-up visit [48].

Studies have also examined the characteristics and conditions associated with receipt of other forms of postpartum contraception. Cesarean delivery and older age are consistently associated with increased likelihood of sterilization [49]. There is also evidence that women with public insurance, such as Medicaid, are more likely to undergo postpartum sterilization [50, 51]. Women delivering in the Southern US have a higher prevalence of sterilization than women in other regions [51]. In general, prevalence of postpartum contraception decreases as maternal age increases [52].

Postpartum contraception has become an increasingly important component of obstetric care in the US. The Healthy People 2020 initiative has set a goal of reducing the percentage of pregnancies conceived within 18 months of a previous birth from 33.1% to 29.8%, a 10% overall reduction [32, 53]. The latest national birth certificate data indicates that in 2016 approximately 29% of singleton births to multiparous women were preceded by an estimated birth to pregnancy

interval of less than 18 months [54]. Birth to pregnancy intervals shorter than 12 months are associated with significantly increased odds of neonatal morbidity [55]. Additionally, birth to pregnancy intervals less than 6 months, although quite infrequent, are associated with increased odds of preterm birth, low birthweight, small for gestational age, and infant mortality [33]. Younger women and women with high school or less education are more likely to have short birth to pregnancy intervals [43]. Women who use other moderately effective or less-effective methods are at significantly higher risk for short birth to pregnancy intervals than women who use highly effective forms of postpartum contraception, such as IUDs or implants [43].

Interconnected with the goal of achieving safe birth to pregnancy intervals, postpartum contraception also helps prevent unintended pregnancies. The postpartum period is particularly important because upwards of 70% of pregnancies that occur within the first 12 months postpartum are unintended [43]. Recent research findings indicate that as the birth to pregnancy interval shortens, the percentage of unintended pregnancies increases, with the highest levels of unintended pregnancy occurring among birth to pregnancy intervals of 0-5 months [56]. Unintended pregnancies have been linked to poorer maternal and infant health outcomes including lower levels of prenatal care, higher odds of preterm birth, higher odds of postpartum depressive symptoms, and lower rates of breastfeeding [57, 58].

There is limited research exploring how maternal comorbidities and infant outcomes potentially influence postpartum contraceptive use. The findings from a 2015 study suggest that women experiencing an extremely preterm birth (gestational age of ≤27 weeks) were more likely to report using no postpartum contraception than women who did not experience an extremely preterm birth [59]. In a second study of the impact of preterm birth, 54.6% of women with preterm births were using no method or low-efficacy methods including male condoms and

withdrawal, though the majority reported not wanting to get pregnant in the first 12 months postpartum [60]. In this sample of women who experienced a preterm birth, the strongest predictor of desiring a pregnancy in the first 12 months postpartum was an infant death (OR:18.2, 95% CI: 8.9-37.0) [60]. In a study of postpartum women in North Carolina, researchers found that women with a recent preterm birth were less likely to receive any contraception compared to women with a term birth; they were also less likely to receive a highly effective method [61].

The results of qualitative studies suggest that women with critically ill infants are at risk for delayed or inadequate postpartum care, typically because they are focused on the health status of their infant [62]. In a study of women with medically complex births, study authors reported high interest in highly effective contraceptive methods, but similar rates of subsequent unintended pregnancy compared to women with low-risk pregnancies [63]. Although these studies are limited in scope, they suggest that women who experience poor birth outcomes such as preterm birth or admission of their infant to the neonatal intensive care unit, may be less likely to use postpartum contraception. Very few studies have examined how complications in the infant due to fetal drug-exposure, such as neonatal abstinence syndrome (NAS), may impact the use of postpartum contraception. The findings from a study from a single, high-risk obstetric clinic in North Carolina indicated that NAS was not a significant predictor of postpartum contraception use; however, the sample size was quite small (n=96) [64].

2.4 Opioids and Opioid Use Disorder

The current opioid epidemic in the United States began in the late 1990s, recognized by a steady rise in overdose deaths related to prescription opioids, which continued through the late 2000s [65]. In 2010, a sharp rise in overdose deaths involving heroin began, coinciding with a

plateauing of overdose deaths related to prescription opioids [65]. Beginning in 2013, in conjunction with the continued rise in heroin-related deaths, deaths involving synthetic opioids such as fentanyl rose precipitously and continued to increase thereafter [65]. In 2017 alone, nearly 48,000 Americans died from opioid-involved overdoses, with a rate of 14.9 opioid-involved overdose deaths per 100,000 population, representing a 12% rate increase from 2016 [66, 67]. Recent evidence, however, suggests that overdose deaths from opioids are plateauing [68]. Between 2017 and 2018, overdose deaths from all opioids decreased 2% ($p<0.05$), with further decreases in deaths due to prescription opioids (14.5% decrease) and heroine (4.1% decrease) [68]. Deaths involving synthetic opioids increased 10% ($p<0.05$) from 2017 to 2018 [68].

Opioids encompass a broad array of chemically related substances [69]. All opioids work by binding to chemical receptors located in the brain, central nervous system, and gastrointestinal tract. While the mechanism of action is similar for all opioids, there are distinct classes of the drug with important implications for potency and use. The first class of opioids are endogenous opioids produced by the human body such as endorphins [70]. Natural opioids, the second class, are exclusively derived from the poppy plant and include morphine and opium [70]. Semisynthetic opioids are derivatives of natural opioids, including heroin, oxycodone, and buprenorphine [70]. Finally, fully synthetic opioids are completely human-made and include methadone and fentanyl [70]. The classes of opioids are further distinguished by varying pharmacological characteristics such as their half-life, lipid solubility, and pharmacodynamic strength. In clinical settings, opioids are commonly used for pain control ranging from acute pain management following surgery to more long-term pain associated with malignancy. Along with pain control and sedation, opioids are known to induce feelings of euphoria which is often

the motivation for misuse and abuse. Other effects of opioids include respiratory depression and constipation [70].

Opioid use disorder (OUD) is defined by the DSM-5 as a "problematic pattern of opioid use leading to clinically significant impairment or distress" [71]. Within psychiatry, OUD is clinically identified using a scale that includes eleven behaviors and patterns associated with OUD [72]. Some behaviors include taking opioids in increasing amounts, experiencing cravings for opioids, and making substantial lifestyle changes to accommodate opioid use [71]. A patient is described as having OUD if they exhibit at least two of the eleven behaviors within a 12-month period, with six or more behaviors classified as severe OUD [72]. OUD, along with other types of SUD, is associated with mental health conditions such as depression and post-traumatic stress disorder, as well as with an increased risk for serious co-morbidities such as HIV, Hepatitis B and C, and endocarditis [73-75]. National surveys estimate that 11.5 million US adults are currently misusing opioids and an additional 1.9 million are currently addicted to opioids [76]. The number of adults with a clinical diagnosis of OUD is significantly smaller, with 1.5 million people having a formal diagnosis of OUD [76].

The demand for OUD treatment in the US has grown substantially over the past decade or so. Between 2005 and 2015, the proportion of substance abuse treatment admissions for opiates increased from 18% to 34% of all admissions [77]. However, the proportion of individuals with OUD who receive any form of substance abuse treatment was low with just 19.7% receiving treatment in 2018 [78]. Increasing access to health insurance that covers substance abuse treatment is one way the federal government has sought to address the opioid epidemic. The Affordable Care Act helped to decrease the proportion of adults with a SUD without health insurance from 25% to 20% in 2014, with the majority of the decrease due to the

expansion of Medicaid in participating states [79]. In 2011, close to 60% of adults aged 26 years and older who sought substance abuse treatment were uninsured, and 20% were insured by Medicaid [80]. Women who entered treatment were less likely to be uninsured compared with men, but the percentage without insurance is high across both groups, 51% of women and 64% of men. Of the remaining adults who entered treatment, nearly 30% of women were covered by Medicaid compared to 17% of men and approximately 10% of both men and women were covered through private health insurance [80].

2.5 Opioid Epidemic and Women

Recognizing the role of sex is crucial for addressing the on-going opioid epidemic. The risk factors for substance use, biophysical pathways of addiction, and response to treatment are significantly different for women than men, but there are similarities in the demographic risk factors for substance use in men and women. Effective research and policy aimed at curbing the opioid epidemic must recognize and address both the biological and social needs and circumstances of women.

The demographic risk factors for substance use among women, particularly opioids, are like those for men. Deaths from opioids among women are highly concentrated among non-Hispanic Whites between ages 25-54 [81]. In fact, opioid-related deaths have become so widespread among this demographic group that these deaths have resulted in a decrease in life expectancy for middle-aged non-Hispanic White men and women in the United States [82]. There are important geographic "hotspots" for opioid deaths, with certain states such as West Virginia, Maryland, and New Hampshire incurring deaths rates from opioids of 30 deaths per 100,000 population, twice as high as the national average of 14.6 [68]. Other demographic risk

factors related to OUD and overdose include low income, unemployment, and low education levels [83].

Although men misuse and overdose from opioids in greater numbers, women have experienced higher rates of increase in opioid misuse and deaths for some classes of opioids. From 1999 to 2016, prescription opioid deaths among women rose 583% compared with 404% among men [66]. During a similar timeframe, deaths from synthetic opioids increased 850% among women [66]. National survey estimates indicate that between 2007 and 2014, heroin use among men increased at an average rate of 8 per 1,000 persons whereas the rate of increase among women was nearly double at 15 per 1,000 persons [84]. The result of a study of overdose deaths among women aged 30-64 showed an increase in overall overdose deaths from 6.7 deaths per 100,000 population in 1999 to 24.3 deaths in 2017 [85]. The rate of overdose deaths involving opioids increased 492% over the same time period, with the largest increases observed among women in older age brackets [85]. Men are more likely to misuse all forms of opioids, but the gender gap has narrowed over the past 15 years [84, 86]. Between 2017 and 2018, deaths from all opioids decreased 4.3% among women, with a smaller decrease of 1.5% observed among men [68].

The rapid increase in opioid misuse and overdose in women can in part be traced to how women experience and report pain, develop drug dependency, and prescribing patterns among physicians. Research highlights the different pathways by which women are introduced to opioids and develop drug dependence. Population-based studies have shown that women are more likely to experience pain, including chronic pain, and are more likely to be prescribed opioids to treat their pain than men [87-89]. A recent study using nationally representative data confirmed that women are significantly more likely to receive prescription opioid analgesics

compared to men [90]. The authors also reported that the difference in prescribing incidence is largely attributable to women experiencing lower socioeconomic status, more adverse health events, and having greater healthcare utilization compared to men [90]. However, trends in prescribing patterns indicate that physicians have begun to decrease both the frequency and dosage of prescription opioids, with opioid prescriptions rates falling nearly 37% between 2012 and 2018, from 81.3 opioids per 100 persons in 2012 to 51.4 in 2018 [91-93]. The underlying mechanisms for the sex differences in both prevalence and intensity of pain, however, are not well understood and are an area in need of further research [89, 94].

Women have also been found to use prescription opioids in higher doses and for longer periods of time than men [95]. There is evidence that women progress to opioid dependence more quickly than men and experience stronger cravings once dependent [96]. The "telescoping effect", seen in alcohol abuse, suggests that women progress more quickly to substance dependence because of physiological differences in body composition, hormonal concentrations, and metabolic rates [97]. While the telescoping effect has been observed in women in relation to opioids, the research is limited and has primarily focused on alcohol use [97, 98]; even with alcohol use, findings are not supported by strong empirical evidence.

Beyond sex-based physiologic differences, there are important social risk factors that distinguish the development and persistence of opioid dependence among women from that in men. Substance use in women is often associated with current or past trauma and violence, where substance use may be a coping mechanism to help women deal with negative emotions and experiences [96]. For example, findings from a large study examining intimate partner violence and substance use indicated that OUD was significantly associated with being a victim of intimate partner violence (IPV) (aOR: 3.27, 95% CI: 2.61-4.09) [99]. Qualitative studies have

also noted that women cope with IPV through substance use and that both physical and emotional abuse can interfere with women's recovery efforts [100]. Substance use in women is also strongly associated with a history of childhood abuse, both sexual and physical, and reported levels of trauma among women with SUD are significantly higher than both the general population and men with SUD [101]. The findings of a recent study of obstetric outcomes among pregnant women with OUD showed a very high prevalence of sexual (56.6%) and physical abuse (65.5%) among the study participants [102].

Mental illness among women with SUD also is an important factor in OUD. In general, women are more likely to experience a diagnosable mental illness with a past-year prevalence of 22.3% in women compared with 15.1% in men in 2017 [103]. A recent study examining data from the National Survey on Drug Use and Health from 2015-2017 reported that among adults with OUD, men were significantly less likely to experience any co-occurring mental illness (aOR = 0.39, 95% CI:0.26–0.57) including serious mental illness (aOR = 0.47, 95% CI:0.32–0.69) compared with women [104]. Results from a randomized controlled trial of adults with OUD indicated similar results with women participating in the trial being 1.6 times more likely to have a co-occurring psychiatric disorder than men [105]. In a large randomized trial of OUD patients, 45% of women reported ever experiencing psychiatric problems compared with 24% of men [96]. Similar to the hypothesis surrounding trauma and drug use, many of these psychiatric problems precede a woman's drug use and drugs may be used as a form of self-medication [96]. It is difficult, however, to separate the cause and effect in this association.

The unique needs and circumstances of women with SUD extend to treatment and rehabilitation. With the dramatic rise in opioid use over the past two decades, there is a well-documented disparity between rates of opioid dependence and the availability of treatment [106,

107]. The shortage of treatment is even more acute among women because less than half of treatment programs offer specialized programs for women and only 23% provide treatment for pregnant or postpartum women [108]. Historically, drug treatment programs have been designed to address the clinical profile and needs of men with SUD; yet, women who present for substance abuse treatment often have more severe medical, psychological, and social problems than men [109]. Women with SUD also face increased social stigma and discrimination compared with men [110].

Services often do not address the specific needs of women with SUD. In 2018 only 26% of substance abuse programs provided targeted services for victims of sexual abuse and intimate partner violence, both of which occur at high levels among women with SUD [108]. Among women who enter substance abuse treatment, 70% have children and yet very few rehabilitation programs allow for children to accompany their parents while receiving treatment [111]. The lack of treatment options designed to accommodate women, both in their life circumstances and their clinical profile, may help explain why women report significantly lower utilization of treatment than men [112-114]. In general, the findings of research evaluating the effectiveness of gender-specific treatment programs verse standard treatment are inconsistent; however, substance abuse programs designed to address co-occurring problems more common in women, such as concomitant psychiatric disorders or experiences of abuse, demonstrate higher effectiveness among these sub-populations [113].

The risk of relapse is an important component of understanding the opioid epidemic and its impact on women, particularly within the context of pregnancy. There is growing consensus among medical professionals that OUD and other SUD are chronic brain diseases, with relapse rates of approximately 40-60%, rates similar to those of other chronic disease such as asthma and

hypertension [115, 116]. Research findings suggest that women are more likely to relapse than men and may relapse at more frequent intervals [117]. The reasons for the increased risk of relapse in women are complex and may be due to both the tendency for women to report more severe withdrawal symptoms while trying to quit and a lack of social support; men who are in the process of recovery are more likely to receive social support at home, at their places of employment, and from their partners [117-120].

The postpartum period is an especially vulnerable time for women with SUD and is considered a period when they are at high-risk for relapse. Findings from a 2015 randomized trial among pregnant women who reported using alcohol or illicit substances indicated that 80% of women who were drug-abstinent in the last month of pregnancy relapsed to at least one substance over the postpartum period [121]. In a recent study examining rates of opioid overdose in the year prior to delivery and the first year postpartum, women with OUD were at the highest risk for overdose in the first 7-12 months postpartum [122]. This finding highlights the importance of providing access to contraception throughout the recovery process, especially during the postpartum period when both stress and risk of relapse are elevated.

2.6 Opioid Use During Pregnancy

Opioid use during pregnancy and pregnancy-related deaths involving opioids have increased in tandem with the opioid epidemic in the United States. This rise in OUD at the time of delivery and during pregnancy has been documented using various data sources, including insurance claims databases, national surveys, and admissions to drug rehabilitation facilities. Taken together, there is clear evidence that opioid use during pregnancy is a growing and significant problem in the US.

There is a spectrum of opioid use during pregnancy ranging from women who use illicit forms of opiates or use prescription opioids for nonmedical purposes during pregnancy, women who are in treatment and using opioid maintenance therapy drugs such as methadone and buprenorphine, and those who obtain medically legitimate prescription opioids from their clinician. While any opioid use during pregnancy carries risk, it is important to distinguish between these groups for the purposes of discussing the prevalence of opioid use during pregnancy, the risk factors associated with each type of opioid use, and for the development of effective interventions.

One of the first studies to examine how the opioid epidemic has impacted maternal mortality at a national level is a recent analysis of national vital statistics data between 2007-2016 [123]. The study findings indicate that pregnancy-associated mortality ratio involving opioids increased from 1.3 to 4.2 pregnancy-associated deaths per 100,000 live births [123]. Gemmill and colleagues also found that the percentage of all pregnancy-associated deaths involving opioids increased from 4% to 10% [123]. Evidence from Utah supports the trends observed by Gemmill and colleagues at the national level. From 2005 to 2014, drug-related deaths were the leading cause of pregnancy-associated mortality in Utah, with 77% of drug-related deaths attributable to opioids [124]. Over the same time period, the drug-related pregnancy-associated mortality ratio increased 200%, along with a 76% increase in the overall pregnancy-associated mortality ratio [124]. Drug-related pregnancy-associated deaths were significantly more likely to occur in the postpartum period compared to deaths due to other pregnancy-associated causes, underscoring the vulnerability to relapse during to the postpartum period [124].

Emerging research results indicate that the opioid epidemic also is a significant contributor to rising maternal morbidity rates in the US [125]. The findings of a recent study using the National Readmissions Database showed that women who used opioids during pregnancy had nearly a three times higher odds of having a postpartum hospital readmission than women who did not use drugs (aOR: 2.86, 95% CI: 2.49-3.29) [126]. The study authors also noted that women who used opioids had a significantly higher obstetric comorbidity index at the time of delivery [126]. The authors of a study of a state-wide inpatient database in North Carolina reported similar increases in maternal morbidity among women who used opioids during pregnancy [127]. Women who used opioids were more likely to experience early onset of delivery, threatened preterm labor, premature rupture of membranes, and had significantly longer hospital stays compared to women who did not use opioids [127]. A recent study of birth outcomes among women with prescription opioid exposure during pregnancy reported that women who used prescription opioids had higher obstetric risk scores and more comorbid conditions than women who did not use prescription opioids [128]. However, the directionality of the relationship between opioid use during pregnancy and maternal morbidity is difficult to ascertain.

The authors of a study based on data from the National Inpatient Sample (NIS) noted a significant increase in the prevalence of opioid use disorder at the time of delivery, rising from 1.5 to 6.5 cases per 1,000 delivery hospitalizations between 1999 and 2014 [129]. A second study, also using the NIS, examined OUD diagnoses in antepartum and delivery hospitalizations, and postpartum hospital readmissions from 1998 to 2014 [130]. The proportion of hospitalizations with an OUD diagnosis increased significantly for all three types of admissions;

antepartum and delivery hospitalizations with an OUD diagnosis were associated with significantly higher risk for severe maternal morbidity [130].

Several prevalence studies of opioid exposure during pregnancy have been conducted among pregnant Medicaid populations [131-133]. All have observed an increasing prevalence of opioid prescriptions among pregnant women. In a national Medicaid sample, codeine and hydrocodone were among the top 10 most commonly prescribed medications for pregnant women from 2000 to 2007 [133]. Over this same time period, the proportion of pregnancies with a prescription for hydrocodone doubled from just below 6% in 2000 to nearly 12% in 2007 [133]. In a second study focused exclusively on opioid prescriptions, the authors reported that 21.6% of pregnant women enrolled in Medicaid filled at least one prescription for an opioid during their pregnancy [131]. A smaller proportion of pregnant women, 2.5%, were chronically exposed to prescription opioids, defined as having an available supply of prescription opioids for 30 days or more during pregnancy [131]. Prescribing patterns varied substantially by state with the lowest prescription rate at 9.5% in New York and the highest at 41.6% in Utah [131]. Over the study time period, opioid prescriptions during pregnancy increased from 18.5% in 2000 to 22.8% in 2007 (p for trend <0.001) [131]. In a second study, restricted to Tennessee Medicaid patients, 29% of pregnant women filled an opioid prescription at some point during pregnancy [132]. Within the study cohort, any opioid use during pregnancy increased 90% between 1999 and 2009 [132].

Prevalence estimates are also available for commercially insured pregnant women. In a national sample from i3 InVision^{TM} for Data Mart, 14.4% of women were prescribed an opioid at some point during pregnancy and 6% of pregnant women received prescription opioids during all three trimesters of pregnancy [134]. The percentage of pregnant women prescribed an opioid

during decreased over the study period from 14.9% in 2005 to 12.9% in 2011, which may reflect larger changes in opioid-prescribing patterns of physicians during this time period [134]. Again, stark geographic differences emerged with women living in the Northeast having the lowest prevalence of opioid exposure while women in the Southern states, including Arkansas, Mississippi, and Alabama had the highest prevalence. There was a two-fold difference in the average prescribing rates of the states in the lowest (10%) vs the highest (20%) prescribing quartile [134].

Other studies have sought to estimate changes in opioid use during pregnancy using data sources other than health insurance claims. The results of a small study from the Mayo Clinic indicated that chronic narcotic pain medication use increased significantly among pregnant women delivering at the hospital from 1998 to 2009 [135]. Over the study time period, the rate of narcotic pain medication use increased from 2.2 cases per 1,000 deliveries to 12 cases per 1,000 [135]. State-level data from Maine revealed a significant increase in OUD at the time of delivery, increasing from 22.7 cases per 1,000 livebirths in 2009 to 34.9 cases in 2018 [136]. Women with OUD at the time of delivery were also more likely to have hepatitis C, concomitant substance use disorders, and depression [136]. In a novel approach to measuring drug use during pregnancy, Martin et al. explored trends in drug treatment admissions among pregnant women for prescription opioid abuse [137]. The percentage of pregnant women admitted to drug treatment facilities as a proportion of all female admissions was stable at 4% nationally from 1999 to 2012 [137]. The proportion of pregnant admissions with prescription opioid abuse, however, increased from 2% to 28% [137]. The authors also found that among admissions during pregnancy, the proportion referred by the criminal justice system increased from 11% to 17% [137].

The National Survey on Drug Use and Health (NSDUH) provides one of few opportunities to estimate nonmedical and illicit use of opioids during pregnancy among a nationally representative sample [138]. Between 2005-2014, 5% of pregnant survey participants reported nonmedical prescription opioid use in the past 12 months and 1% reported nonmedical use in the past 30 days [138]. The 2012 NSDUH found that among pregnant survey participants, 5.9% reported current illicit drug use including heroin, fentanyl, and other street drugs compared with 11.4% among non-pregnant women aged 15-44 years [139]. Beyond these national survey estimates, there is little national data on the frequency of illicit drug use during pregnancy. The prevalence of Hepatitis C virus (HCV) at the time of delivery has mirrored the trends of opioid use and OUD during pregnancy. From 2000-2015, the rate of HCV infection among all hospital deliveries in the US increased from 0.8 to 4.1 cases per 1,000 deliveries [140]. Among deliveries to women with OUD, the prevalence of HCV infection increased from 87.4 in 2000 to 216.9 cases per 1,000 deliveries in 2015 [140]. This surge in HCV infections among pregnant women, and particularly those with OUD, are a significant consequence of the opioid epidemic, particularly as it relates to the health impact on women and infants.

The risk factors and correlates of opioid use during pregnancy are complex and diverse. This diversity is in part due to the heterogeneous population that falls under the broad umbrella of opioid use during pregnancy. Pregnant women with nonmedical prescription opioid use and who use illicit opioids, such are heroin, have the greatest risk burden. Pregnant women with OUD often have lower levels of prenatal care than women without OUD during pregnancy [141]. Demographically, pregnant women with OUD are more likely to be non-Hispanic White, younger, unmarried, low income, have not completed high school, and to be publicly insured or uninsured [138]. Pregnant women with OUD are also more likely to experience numerous

significant comorbidities. Psychiatric comorbidities including depression and anxiety are highly prevalent in this population as are non-opioid substance use disorders [142]. Pregnant women with nonmedical prescription opioid use in the past year have significantly higher prevalence of anxiety and depression diagnoses, and more frequently report alcohol, tobacco, and marijuana use based on data from the NSDUH from 2005-2014 [138]. This same study reported that the strongest predictors of nonmedical prescription opioid use in pregnant women were depression or anxiety diagnosis within the past year (aOR: 2.15, 95% CI: 1.52-3.04) and marijuana use within the past year (aOR: 3.44, 95% CI: 2.47-4.81) [138].

The recommended treatment for women diagnosed with OUD during pregnancy is a combination of pharmacotherapy and behavioral counseling [143]. In fact, both ACOG and SAMHSA strongly advise against opioid abstinence and medically assisted withdrawal because of the high risk of relapse and obstetric complications [143, 144]. Pharmacotherapy, also known as medication assisted therapy (MAT), is an important component of treating pregnant women with OUD because it helps prevent symptoms of opioid withdrawal which in turn decreases the risk of relapse to illicit opioids, increases adherence to prenatal care, and decreases the risk of obstetric complications [144, 145]. A meta-analysis found that women undergoing medically supervised detoxification during pregnancy have a 1.91 (95% CI: 1.14, 3.21) times higher risk of relapse compared with women on MAT [146].

There are two primary drugs used to treat OUD during pregnancy; methadone and buprenorphine, both of which act as full or partial opioid agonists [143, 147]. Opioid agonists act on the same receptors as other forms of opioids but are dispensed in highly controlled, therapeutic doses designed to limit withdrawal symptoms [143]. Buprenorphine may be favored over methadone because of its limited potential for overdose, and lower observed rates of NAS;

buprenorphine also does not require daily, supervised administration like methadone [143]. Both drugs can cause NAS in infants; however, evidence indicates that buprenorphine results in less clinically significant NAS in infants compared with methadone [143, 148, 149]. Naltrexone, an opioid antagonist which blocks the euphoric effects of opioids, is a third FDA-approved pharmacological OUD treatment option. Unlike methadone and buprenorphine, naltrexone requires full detoxification from opioids before it can be used. For this reason, naltrexone is not recommended for use during pregnancy, but has been used to successfully treat OUD in nonpregnant persons [143, 150].

There is growing evidence that Naltrexone may be a safe and viable treatment option for pregnant women with OUD, including significant decreases in NAS diagnoses, decreased infant hospital length of stay, and reduced opioid misuse during pregnancy [151, 152]. A recent study examined pregnancy outcomes among pregnant women receiving MAT, comparing naltrexone with methadone/buprenorphine [152]. The study authors reported significantly lower levels of NAS among infants born to women using naltrexone than among infants born to mothers using methadone/buprenorphine (8.4% vs 75.2%, $p<0.0001$). While postpartum relapse rates were not captured, there were no relapses during the mandatory detoxification period for women using naltrexone [153].

2.7 Neonatal Abstinence Syndrome

Fetal exposure to opioids has garnered significant public attention as one of the most troubling consequences of the opioid epidemic. The evidence is inconsistent, however, regarding the risk of preterm birth and low birth weight among infants with prenatal opioid exposure [154]. The results of a recent study from the Boston Birth Cohort indicated that opioid-exposed births had significantly higher odds of fetal growth restriction (OR: 1.87, 95% CI: 1.41-

2.47) and preterm birth (OR: 1.49, 95% CI: 1.19-1.86) [155]; however, caution must be exercised in interpreting these results because 60 percent of the opioid exposed births had a diagnosis of NAS and some important covariates were not adjusted for such as use of other substances during pregnancy. There is some evidence that these infants may be at increased risk for some congenital anomalies and fetal death [143, 154, 156].

The most commonly cited sequalae of fetal opioid exposure is neonatal abstinence syndrome (NAS) which results from the sudden interruption of fetal substance exposure at the time of delivery. While NAS is most often associated with fetal exposure to opioids, several antipsychotic drugs, methamphetamines, and inhalants are also associated with NAS [157]. Terminology more specific to fetal opioid exposure is becoming increasingly common including Neonatal Opioid Withdrawal Syndrome (NOWS); however, NAS diagnosis is still used for the purposes of administrative coding. NAS is characterized by a constellation of symptoms including gastrointestinal issues, irritability, high-pitched cry, poor sleep, difficulty feeding, tremors, and in rare cases, seizures [158].

Among women who use opioids during pregnancy, the observed frequency of NAS has ranged from 5% to 94%, with the highest observed levels among women using methadone and heroin [157]. Since 2000, the incidence of NAS among US births has increased substantially, with notable geographic variation. Two recent studies examined this increasing incidence: the results of one study showed that between 2009 and 2012, NAS increased from 3.4 cases per 1,000 hospital births to 5.8 cases [159]; in a second study among 28 states, NAS incidence rose from 1.5 cases to 6.0 cases per 1,000 hospital births between 1999-2013 [160]. The steep increase in NAS cases corresponds to national trends indicating increased use of opioids during pregnancy [129]. Beyond the increase in frequency, the severity of NAS cases is also a concern.

The proportion of NICU admissions attributable to NAS has increased from 7 cases per 1,000 NICU admissions in 2004 to 27 cases per 1,000 NICU admission in 2013 [161]. Once admitted to the NICU, the median length of stay for these infants increased from 13 days to 19 days over the same time period [161]. There also been a rise in the proportion of NAS infants receiving pharmacological support, often an indication of heightened severity [161].

NAS is associated with all classes of opioids including opioid maintenance drugs such as methadone and buprenorphine. The onset, duration, and severity of NAS is influenced by several factors including the time of last substance exposure, duration of fetal exposure, and total aggregate exposure. Factors beyond exposure to opioids can also influence NAS outcomes such as maternal smoking and poly-substance use, both of which are common among women who use opioids during pregnancy [157] [162, 163]. Because opioids can accumulate in fatty tissue, infants born full-term or infants with a birth weight of 2,500 grams or higher are more likely to experience severe and prolonged NAS symptoms [157].

Although there are several methods used to assess NAS, the most commonly used clinical tool in the US is the modified Finnegan scoring system [164]. In conjunction with the scoring system, toxicological tests of infant urine or meconium can confirm recent substance exposure. Management of NAS is often a dual approach using pharmacological and nonpharmacological interventions. In all cases, nonpharmacological treatments are used including gentle handling, on-demand feedings, swaddling, and low-stimulation environments, all of which have been shown to improve NAS symptoms [164]. In more severe cases, pharmacological support is necessary, with morphine the most commonly used medication to support infants when needed [161].

Evidence of the long-term impact of fetal exposure to opioids on child development is inconclusive. There is some evidence that fetal exposure to opioids may be linked to hyperactivity and attention issues in toddlers [158]. Evidence from the Boston Birth Cohort suggests that children with in-utero opioid exposure have higher odds of conduct disorder (OR: 2.13, 95% CI: 1.20-3.77) and attention-deficit/hyperactivity disorder (OR: 2.55, 95% CI: 1.42-4.57), but this study relied on a select follow up sample of infants receiving care at a specific medical center, therefore, results must be interpreted with caution [155]. The result of studies on long term cognition and academic achievement among exposed children are inconsistent and many do not adequately control for confounders [158]. A recent study of Pennsylvania Medicaid claims found that 5-years after birth, children with in-utero opioid exposure were no more likely to be diagnosed with a complex chronic condition than children without in-utero exposure [165]. Isolating the impact of opioid exposure is exceedingly difficult for multiple reasons. Women who use opioids during pregnancy are often polysubstance users, making it difficult for researchers to isolate the impact of opioids on infant and child development. Furthermore, women who abuse substances often experience concomitant risk factors such as poverty, low levels of prenatal care, and stressful home environments all of which influence infant and child development outcomes [166].

2.8 Contraceptive Use and Unintended Pregnancy among Women with Substance Use Disorders

Postpartum contraception is an important consideration for all women, but it is of special importance for women with SUD. Women with SUD experience the same benefits from postpartum contraception, and contraception use generally, as other women of reproductive age. Yet, because women with SUD face additional risks such as substance use relapse, concomitant morbidities, and social disparities, postpartum contraception use can confer additional benefits

by allowing women to focus on caring for themselves, their newborn, and receiving help for on-going issues associated with substance use.

There is a growing body of literature dedicated to describing and understanding contraception use and unintended pregnancy among women with substance use disorders (SUD). Overall, women with SUD have been found to have exceptionally high rates of unintended pregnancy and tend to use less-effective methods of contraception, such as male condoms, compared with the general population [167, 168] [169-171] [172]. Given the US opioid epidemic, research focused on the reproductive, sexual, and obstetric health needs of this population is critical.

Understanding contraception use and contraceptive method choice is a crucial component for improving reproductive health outcomes in women with SUD. A systematic review examined the literature concerning contraception use and unplanned pregnancy among women with SUD [172]. The authors found a median contraceptive prevalence of 55% among women with SUD, with a range of 6%-77% across studies [172]. In the US, the NSFG, a nationally representative survey, reports that 65% of women aged 15-49 are currently using contraception [173]. The systematic review also reported that women with SUD more frequently relied on less effective methods. Male condoms were the most common primary contraceptive method among women with SUD (62%) whereas just 9.4% of the general US population report using condoms as their primary contraceptive method [172, 173]. In a study among low-income women in Massachusetts, women with SUD were significantly less likely to use any form of prescription contraception compared with women without SUD (aOR: 0.79, $p<0.001$) [170]. Among those who did use prescription contraception, women with SUD were significantly less likely to use

the most effective forms of prescription contraception, such as the IUD or implant, than women without a SUD (aOR: 0.83, $p<0.05$) [170].

A recent study examined contraceptive health insurance claims among privately insured, non-pregnant women of reproductive age who were identified as filling chronic opioid prescriptions [174]. The authors reported that among the 16,074 women aged 15-44 who were identified as filling chronic opioid prescriptions, 23.4% had a contraceptive claim in the 270 days before or after the initial opioid prescription [174]. The study authors concluded that the relatively low contraceptive prevalence may indicate unmet need in this population: however, the study is subject to significant limitations because the 9-month study timeframe reduced the accurate identification of long-acting forms of contraception such as the IUD and implant [174]. A study among women receiving care at two MAT clinics in Tennessee reported that 53% of women had experienced an unintended pregnancy; although 90% of women reported wanting to avoid pregnancy, only 59% were regularly using contraception [175].

Studies in high-resource settings outside of the US indicate large disparities in contraceptive use among women with SUD. In a British cohort of women receiving MAT, the overall contraceptive prevalence was 30% compared with the national U.K. average of 75% [169]. Women receiving MAT also had significantly lower usage of prescription contraceptives compared to the national U.K. average (24% vs 50%, $p<0.001$) [169]. Among women attending public opioid treatment programs in Australia, 54.7% reported use of any contraception with the most popular methods being male condoms followed by the pill [168]. The literature has consistently shown that women with SUD tend to use contraception at lower levels than the general population and when they do so, male condoms are often the primary method.

Women with SUD have consistently higher rates of unintended pregnancy, abortions, and stillbirth compared with the general population [127, 167, 170]. A 2016 systematic review indicated that the unintended pregnancy rate among women with SUD ranged from 80%-85% compared with 45% in the general US population [4, 167]. In a study involving opioid abusing pregnant women in the US, the study authors reported that 86% of pregnancies were unintended [171]. The results of a study in Connecticut involving pregnant women with SUD revealed similar levels of unintended pregnancy with 80% of women indicating their pregnancy was unintended at study entry [176]. A medical record review of women with OUD and two consecutive deliveries at a medical center in Vermont, reported that 84% of the pregnancies were unplanned [177]. Among a sample of Australian women attending an opioid treatment program, study authors reported a lifetime average of 4.6 pregnancies per woman [168]. Among women who experienced a pregnancy within the last 12 months, 75.5% of these pregnancies were classified as unplanned [168]. A cohort of British women receiving treatment for opioid addiction were observed to have substantially higher rates of pregnancy terminations when compared with the national average (0.46 abortions per study participant vs 0.025 abortions per aged match woman nationally) [169].

There is evidence that women with SUD have higher rates of miscarriages and stillbirths compared with the general population [127, 167]. Australian women in the sample attending an opioid treatment program had higher rates of miscarriage, stillbirth, and abortion than a national sample of Australian women [167]. A recent study of inpatient hospitalizations among women who used opioids during pregnancy in North Carolina found that opioid use was associated with 50% increased odds of stillbirth (aOR: 1.5, 95% CI: 1.8-2.3), along with several other serious maternal and fetal complications [127].

The observed rates of unintended pregnancy among women with SUD suggest there may be substantial unmet need for contraception among this group, defined as the proportion of women at risk for unintended pregnancy who are not using contraception. Preliminary data from a substance abuse treatment center in Michigan indicates that only 37% of women at risk for unintended pregnancy were using any form of contraception and only 37% of that group were using a highly effective form such as an IUD, implant, or sterilization [178]. More research is needed to understand the extent of unmet contraceptive need among women with SUD and the barriers that prevent women with SUD from accessing or consistently using contraception.

Relatively little is known about postpartum contraception use among women with SUD. Measurement of postpartum contraception use often varies in terms of follow up time and ability to measure the full range of contraceptive methods. Studies that rely on insurance claims data are restricted to examining prescription methods of postpartum contraception and cannot capture condom use or other non-prescription contraceptive methods. The few studies focused on postpartum contraception among women with SUD have reported varying prevalence levels.

Among PRAMS respondents in Tennessee, women who used drugs were less likely to report using any postpartum contraception (79.6% vs 88.1%, p-value<0.05) and had significantly lower odds of postpartum contraception use than women who did not use drugs (aOR: 0.54, 95% CI: 0.29-0.99) [179]. In a recent study using Pennsylvania Medicaid claims data, 74.5% of postpartum women with OUD were not using prescription contraception, which included female sterilization, IUD, implant, DMPA, the pill, patch, or ring, within the first 3 months postpartum [180]. Overall, 7.4% of women with OUD were using a highly effective method, defined as female sterilization, IUD, or implant, within the first 3 months postpartum [180] in contrast to a

study of a general population of Medicaid-enrolled postpartum women, in which 16.4% were using a highly effective form of postpartum contraception [181].

In a separate study also based on Pennsylvania Medicaid claims for women with OUD at the time of delivery, the authors examined whether Medicaid expansion impacted postpartum health care utilization by measuring changes in postpartum visit attendance and receipt of postpartum contraception [38]. The Pennsylvania Medicaid expansion included a provision extending health insurance coverage for postpartum mothers from 60 days to 300 days postpartum. Despite an increase in length of coverage, there was no change in the percentage of women attending a postpartum care visit within 60 days (15% pre-expansion; 16.4% post-expansion) [38]. Similarly, the authors did not observe a change in the percentage of women using postpartum contraception at either 60 days (23.5% pre-expansion; 21.0% post-expansion) or 300 days postpartum (39.3% pre-expansion; 37.5% post-expansion) [38]. In both the pre- and post-expansion periods, postpartum visit attendance and postpartum contraception use were exceptionally low in this population of postpartum women with OUD.

A recent study examined receipt of LARC among women with OUD who are currently using MAT [182]. Among women with an intention to use postpartum LARC, 18% received a LARC method by eight weeks postpartum [182]. In adjusted models, prenatal contraceptive counseling was significantly associated with prenatal LARC intent (aOR: 6.67, 95% CI: 3.21-13.89) whereas receipt of prenatal care from a private practice provider was associated with a significant reduction in prenatal LARC intent (aOR: 0.48, 95% CI: 0.32-0.72) [182]. The authors also noted low postpartum visit attendance among the cohort, with 30% of women attending a postpartum care visit within the first eight weeks postpartum. In comparison, approximately 50% of Medicaid-insured women without OUD attended a postpartum visit [181].

Prior research indicates that postpartum visit attendance is strongly associated with postpartum contraception use, particularly LARC [183].

Krans and colleagues also examined repeat pregnancies in their sample of Medicaid-enrolled postpartum women with OUD. They found no significant difference in time to the next pregnancy comparing women using no prescription contraceptive method and those using a user-dependent prescription method (e.g. pill, patch, ring, DMPA injection); women using a highly effective method, however, had a significantly lower hazard of subsequent pregnancy [180]. The findings of a second study involving postpartum women with SUD indicated that approximately 30% of women reported no contraceptive use over the course of a 24-month follow up [176]. Among women who reported using postpartum contraception, DMPA injections were the most popular followed by condoms and the pill [176]. The results of a study from Vermont among women with OUD revealed that 56% of study participants had a birth to pregnancy interval less than 18 months and 50% of women did not receive any contraceptive method during the postpartum period [177]. Finally, a 2014 study examined the effectiveness of contraceptive counseling for postpartum women on MAT [64]. Study authors reported that upon hospital discharge, 40% of women were using contraception and another 45.7% had a documented plan for postpartum contraception [64].

2.9 Study Rationale

Prior research focused on postpartum contraception provision among women who use opioids during pregnancy is limited in quantity and scope. Previous literature has generally focused on women insured by Medicaid, women with OUD, or women enrolled in substance use treatment programs and research trials [38, 64, 176, 177, 180, 182, 184]. Furthermore, much of this research lacks a comparison group of women who did not use opioids during pregnancy,

limiting generalizability and failing to provide a broader understanding of contraception use among women who use opioids compared to the general population. This study addressed several of these limitations. Foremost, the current research examined a large sample of privately insured women who are often omitted from substance use research. The study included a comparison group of women with no evidence of opioid use during pregnancy, providing context for how contraceptive provision among women who use opioids compares to the broader, privately insured population.

This study also disaggregated by type of opioid used during pregnancy in relation to postpartum contraceptive use. Three categories of opioid use were examined: non-chronic prescription opioid use, chronic prescription opioid use, and formal diagnoses of opioid use disorder or buprenorphine prescriptions. Women in each opioid use category has a distinct clinical and demographic profile, highlighting the need to disaggregate by type of opioid use. These strengths addressed a current gap in the literature and provide nuance in understanding how demographic, clinical, and behavioral characteristics differ across categories of opioid use as well as how they relate to postpartum contraceptive provision.

In addition to expanding the scope compared to prior research, this study capitalized on the longitudinal nature of the data source to include variables from the pre-, peri-, and postnatal periods. Previous research reliant on inpatient hospitalization records or other cross-sectional data sources did not examine diagnoses during the prenatal period or outpatient pharmaceutical claims to identify women who use opioids during pregnancy [127]. While the current study did not include the full-array of demographic characteristics typically included in contraceptive research, the data source allowed for inclusion of a wide-variety of prenatal clinical variables. Clinical outcomes in the infant were also considered in the current study. There are very few

studies that include infant outcomes as covariates in models examining postpartum contraception, although there is research that indicates infant outcomes, particularly adverse outcomes, play a role in postpartum maternal health-seeking behavior [62, 64, 185-187].

The opioid epidemic, while no longer growing at the pace of the mid-2000's, remains a substantial and critical public health crisis [65]. Early state-level reports indicate that the current COVID-19 pandemic may be reversing much of the progress made in recent years in combating opioid-related overdose deaths [188, 189]. Research consistently highlights the pressing need to expand efforts to address the sexual, reproductive, and maternal health needs of women who use opioids [143, 150, 190, 191]. Over the past decade, research on the opioid epidemic has greatly expanded our understanding of how this crisis has impacted women across the US. Despite the heightened research interest, gaps remain in the literature. This research addressed several of these gaps by examining an under-studied population, disaggregating by type of opioid use, leveraging a longitudinal data source to include variables for all stages of pregnancy and postpartum, and analyzed contraceptive provision over the full postpartum period through one year. Each of these strengths improves our understanding of how opioid use during pregnancy impacts postpartum contraceptive provision, a vital component of maternal healthcare.

2.10 Conceptual Framework

The conceptual framework for this research is based on the concepts and elements that are generally thought to influence a woman's decision to use postpartum contraception while also incorporating factors that are unique to women with substance use disorders. The framework presents three, hierarchical layers each containing various factors that influence postpartum contraception use as well as additional factors associated with the complications posed by opioid use during pregnancy.

Factors at the individual level are divided into three broad categories: demographic, psychosocial, and clinical. Demographic factors cover characteristics typically included in contraceptive research in the US such as maternal age, race/ethnicity, parity, income, and relationship status. Frequency of sexual activity is also included within the demographic factors as this may influence or encourage postpartum contraception use. Clinical factors focus primarily on concerns that arise from opioid use during pregnancy and opioid use disorder generally but also include universal clinical considerations such as mode of delivery and common comorbidities. These comorbidities include chronic and gestational hypertension, pre-existing and gestational diabetes, autoimmune disorders, and pain conditions. Pain conditions are an important consideration as they are associated with prescription opioid use. This research also explored if postpartum complications of opioid use during pregnancy, such as an NAS diagnosis in the infant, NICU admission, and infant hospital length of stay, influence postpartum contraceptive provision. Finally, psychosocial factors include conditions and events typically associated with substance use such as unstable life circumstances and experience of abuse as well as factors that are widely generalizable to most contraceptive decision making. Several partner-level psychosocial factors, such as experiences of intimate partner violence (IPV) and partner substance use, are included as these factors are known to influence substance use in women and, particularly in the case of IPV, may influence contraception use [99, 192, 193]. Data about these psychosocial factors, however, were not available for the current study.

A limited number of healthcare system factors were assessed in this research including antenatal and postpartum care visits. Other aspects of the healthcare system are important for contraceptive decision making including the quality of healthcare interactions, affordability and accessibility of contraceptive methods, and past encounters with the healthcare system; these

factors could not be measured in the current study. Evidence suggests that high quality contraceptive counseling in the antenatal period can increase postpartum contraceptive use [34]. However, if a woman has persistently poor or limited interactions with the healthcare system, she may be less inclined to engage with providers about her postpartum contraceptive options. The quality of healthcare interactions as well as past experiences within the healthcare system are particularly important in the case of women who use opioids during pregnancy as they may be subject to stigma from a variety of sources. The quality of healthcare interactions could not be measured in this study, but receipt of antenatal care and a postpartum care visit were included in the analysis.

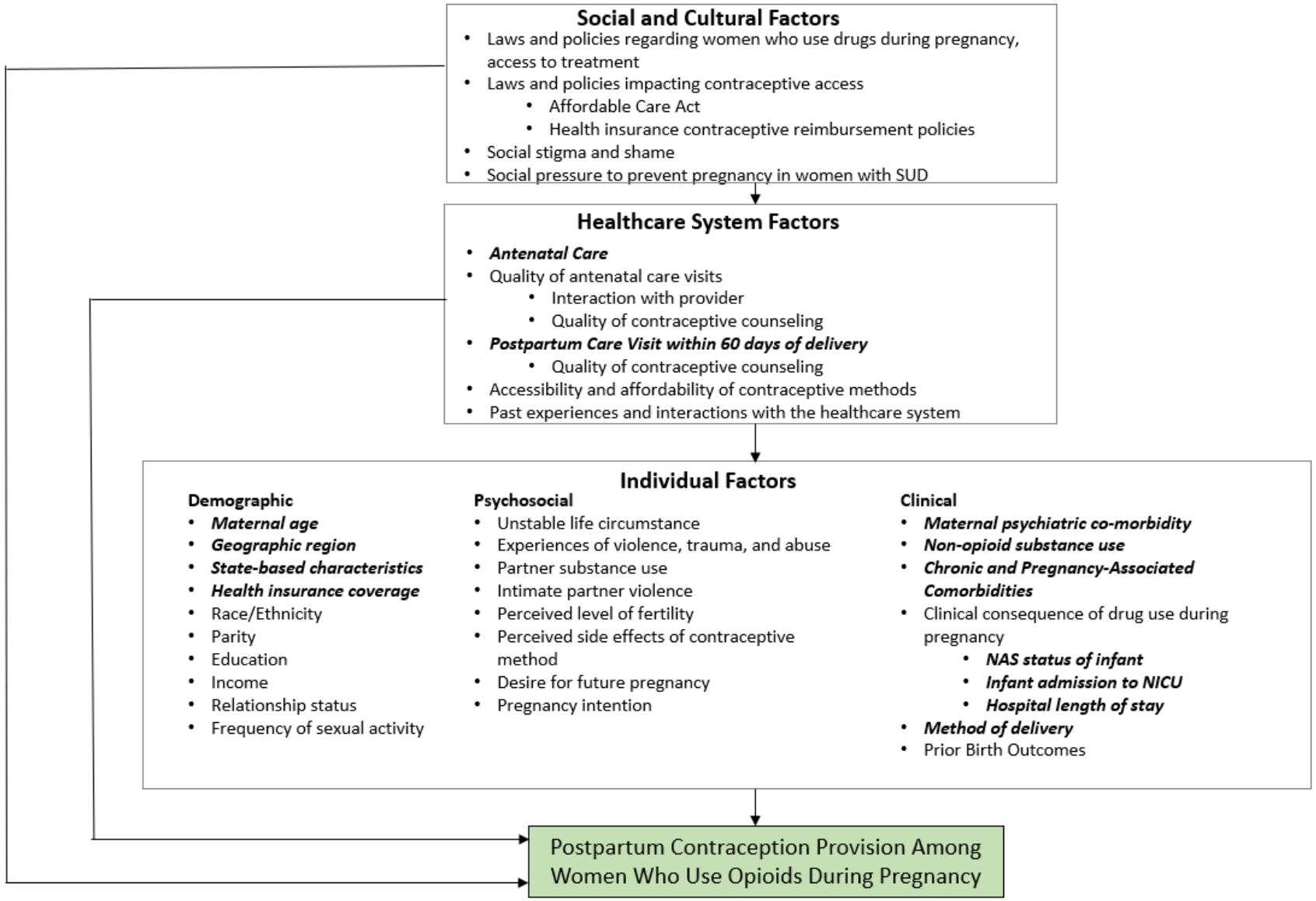
Finally, social and cultural factors that influence postpartum contraception use are broad measures of how society views women who use drugs during pregnancy. The laws and policies directed towards women who use illicit drugs during pregnancy can act as significant barriers to care-seeking as research indicates that women may delay or avoid the healthcare system when punitive laws are in place [194-197]. Furthermore, punitive laws do not decrease the incidence of NAS or maternal substance use which are often the stated goals of these laws and policies [197]. Beyond explicit laws and policies, the shame and stigma attached to drug use during pregnancy may be enough to delay or deter women from seeking care [196, 198, 199]. Women report fear of child protective services, potential criminal justice involvement, and past negative interactions with healthcare workers as barriers to seeking care [196].

Access to contraception is also impacted by laws and policies such as the Affordable Care Act, which has significantly decreased out-of-pocket costs for all reversible prescription contraceptive methods and may be a contributing factor to increased LARC uptake in the US [200]. However, consistent availability of LARC devices and delays in contraceptive placement

continue to impede women's ability to access contraception. Insurance reimbursement policies that support immediate postpartum LARC insertion also play an important role and have been shown to decrease unintended pregnancy and reduce short birth-to-pregnancy intervals [201]. Unlike numerous state-based Medicaid programs, few private insurance companies cover immediate postpartum LARC insertion, making it difficult for privately insured women to obtain LARCs during their hospital stay for delivery [46].

While the conceptual framework presented in Figure 2.1 is comprehensive, the data source for this research was limited in the ability to capture demographic and psychosocial variables but contains extensive clinical measures including varying types of opioid use, a strength of this research. An attempt was made, however, to create state-level variables (race, education and poverty) as proxy measures for the important missing demographic variables. The variables available for inclusion in the current research are presented in bold in the framework. This research is the first to examine the relationship between opioid use during pregnancy, disaggregating by type of opioid use, and postpartum contraception use among a privately insured patients in the US based on a very large sample. Future research should focus on including a broader range of sociodemographic and clinical variables, including parity, maternal relationship status, income, methadone usage, and expanded measures of contraception to include methods that do not require a prescription. The use of alternative data sources, such as linked medical records and insurance claims, may help expand the information available for analysis while retaining the longitudinal scope of the data. This research serves as the initial foundation for understanding the relationship between opioid use during pregnancy and postpartum contraceptive provision among privately insured women.

Figure 2.1. Conceptual Framework



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Chapter 3. Study Design and Methods

3.1 Overview

This chapter describes the data source and study methods used to address the three study aims related to provision of prescription contraception during the postpartum period among women who did and did not use opioids during pregnancy. It begins with an overview of the specific aims, followed by a description of the study design, data source, and study cohort for each study aim. The dependent and independent variables for each study aim are then defined and described. Finally, the analytic plan, including statistical models, are presented for each aim.

3.2 Study Aims

The three study aims were evaluated in a population of privately insured women in the United States (US) with a live birth between January 2011 and November 2017; they were to:

Aim 1: Evaluate the association between opioid use during pregnancy and prescription contraception provision by 60 days postpartum, including by contraceptive method type.

Aim 2: Evaluate the time to first prescription contraception provision during the postpartum period for women who did and did not use opioids during pregnancy, including by type of opioid.

Aim 3: Assess if adverse newborn outcomes are associated with provision of prescription contraception within 60 days postpartum among women who used opioids during pregnancy.

3.3 Study Design

This study was a retrospective cohort study using health insurance claims data for privately insured women in the US who experienced a live birth between January 2011 and November 2017. The initial cohort included all women with a live birth captured in the data source, hereafter referred to as the MarketScan database. Pregnancies that did not end in a live

birth, including ectopic pregnancies, molar pregnancies, stillbirths, and spontaneous abortions prior to 20 weeks gestation were excluded. Several additional exclusion criteria, including length of continuous health and pharmaceutical insurance coverage, were applied to identify the analytic sample for each study aim but the initial cohort of women with a delivery was retained to conduct sensitivity analyses throughout the analysis.

3.4 Data Source

The data source for this study was the MarketScan database which contains paid insurance claims for privately insured patients in the US from 2010 to 2017. The data was collected and compiled by Truven Analytics and later IMB into the MarketScan database. It is comprised of seven separate but linked categories of claims and enrollment data. The database contains paid claims data from 350 payers including commercial insurance companies and third-party administrators, with an estimated total of 100 million individual enrollees. According to the US Census, approximately 67% of American's are insured through private health insurance plans [1].

The Marketscan database is structured by claim and information type which fall into seven categories. These categories include four categories capturing inpatient and outpatient services, one category documenting outpatient pharmaceutical claims, and two categories with demographic and enrollment data for each individual enrollee (Table 3.1). Inpatient pharmaceutical claims are not captured in the Marketscan database. The seven data categories are linked using a unique enrollment ID ("enrolid") for each individual with insurance coverage. This enrollment ID is used to link paid claims across categories within the database and allows researchers to follow patients over time. It links claims for individuals for as long as they have continuous enrollment in a specific health insurance plan, but not across different plans. If, for

instance, an individual receives health insurance through their employer, switches to a new job, and regains health insurance through a new employer, the individual will re-enter the MarketScan Database with a new enrollment ID.

Beyond the individual enrollment ID, there is also a family ID which links claims within a family or group of related people who are receiving health insurance through the same plan. In other words, health insurance claims for the child of a person receiving health insurance through their employer will be linked to the primary beneficiary through the family ID ("efamid"). This family ID was used to link the records of women and their live-born infant during the inpatient admission for delivery for Aim 3. This linkage was important for this research as infant outcomes, including neonatal abstinence syndrome (NAS) diagnosis, admission to the neonatal intensive care unit (NICU), and infant hospital length of stay were included as predictor variables for postpartum contraceptive provision. A final linkage within the database is a unique case ID, which links all inpatient claims associated with a single inpatient admission, such as a hospital admission for a delivery. This case id was used to link NICU admissions for the infant with their overall inpatient admission record at the time of delivery.

Diagnoses and procedures captured within the MarketScan database are coded using standard clinical coding systems. Primary and secondary diagnoses are captured using International Classification of Disease (ICD) codes. Version 9 of the ICD coding system (ICD-9-CM) was used until September 30th, 2015; a switch to ICD-10-CM was made beginning on October 1st, 2015. Procedures are captured and classified using the Current Procedural Terminology, 4th Edition (CPT-4) coding system or the Healthcare Common Procedural Coding System (HCPCS). Prescription drug types are identified using the National Drug Codes (NDC). A comprehensive list of all diagnostic, procedure, and contraceptive drug codes used in this

research can be found in Appendix A. The drug codes used to identify opioids prescription can be found at the Centers for Disease Control website: https://www.cdc.gov/drugoverdose/resources/data.html.

Table 3.1 outlines and describes the seven categories of data contained within the MarketScan Database and how each category was used in the current research. The inpatient admissions data includes a single line for every inpatient admission, including demographic information associated with the patient and up to fifteen separate diagnosis and procedure codes. The inpatient admission records were used to identify several critical variables for this research including the livebirth, all maternal comorbidities, immediate postpartum contraceptive provision, and select infant variables. The inpatient services data is closely related to the inpatient admissions data as the inpatient services data contains individual lines for each diagnostic and/or procedure codes associated with the overall inpatient admission. The inpatient services data is linked to the inpatient admission using the unique case ID assigned to each inpatient admission. The inpatient services data was used to ascertain infant NICU admission.

The outpatient services claims data contains diagnoses and procedures associated with outpatient encounters and was used to identify several variables including postpartum contraceptive provision, maternal comorbidities, and both antenatal and postpartum care visits. The outpatient pharmaceutical data contains records for all paid outpatient pharmaceutical claims. This data was used to determine postpartum contraceptive provision and prescription opioid use during pregnancy. Finally, the annual enrollment data provides month-by-month information on individual health and pharmaceutical insurance enrollment. The enrollment data was used to determine periods of continuous enrollment for the analytic cohorts in Aims 1-3.

Neither the facility header data nor the enrollment detail data were used in this analysis. Table 3.1 summarizes the data categories.

Table 3.1. Summary of MarketScan Data Categories

Data Category	Category Description	Linkage Variable	Application in Current Research
Inpatient Admissions (I)	All encounters and claims linked with a hospital admission Contains the principle diagnosis and procedure code and up to 14 other diagnostic and procedure codes	Cases and services link to inpatient services claims; unique identifier for each inpatient enrollment (CASEID) Linked to all other data categories through enrollment id (ENROLID)	Identify deliveries, all delivery-related variables (maternal age, year, region, mode of delivery) Immediate postpartum contraception, including, female sterilization and LARC Psychiatric diagnoses OUD diagnosis, non-opioid substance use disorder diagnosis Chronic disease Pain conditions Infant hospital length of stay; Infant NAS diagnosis
Inpatient Services (S)	Individual facility and professional services comprised in the inpatient admissions record	Cases and services link to inpatient admissions (CASEID) Linked to all other data categories through enrollment id (ENROLID)	Infant NICU admission
Outpatient Services (O)	Encounters and claims for services obtained in a doctor's office, hospital outpatient facility, emergency room, or other outpatient facility	Linked to all other data categories through enrollment id (ENROLID)	ANC visits, postpartum care visit Postpartum contraception, including female sterilization OUD diagnosis, non-opioid substance use disorder diagnosis

Data Category	Category Description	Linkage Variable	Application in Current Research
			Psychiatric diagnoses Chronic disease Pain conditions
Outpatient Pharmaceutical Claims (D)	Outpatient pharmaceutical claims for prescriptions obtained outside of an inpatient setting	Linked to medical/surgical data (ENROLID)	Opioid prescriptions during pregnancy Prescription forms of contraception
Annual Enrollment (A)	Monthly arrays of enrollment indicators with a single record per-person, per-year	Linked to all other data categories through enrollment id (ENROLID)	Length of continuous enrollment Length of continuous prescription drug coverage
Enrollment Detail (T)	One record per person per month of enrollment containing demographic and geographic information	Linked to all other data categories through enrollment id (ENROLID)	N/A
Facility Header (F)	Complete header information for facility claims	Linked to the inpatient services and outpatient services claims (FACHDID) Linked to all other data categories through enrollment id (ENROLID)	N/A

N/A= Not applicable; indicates a data category not used in the analysis

3.4.1 Strengths and Limitations of the MarketScan Database

The MarketScan database has notable strengths as well as several limitations. Foremost, the MarketScan database is large, providing data on an estimated 100 million privately insured persons in the US. The size and scope of the database allows researchers to examine otherwise rare subpopulations, events, and clinical outcomes. In the case of this research, although opioid use during pregnancy is a rare event in the general population and even more so in the privately insured population, the size of the Marketscan database allowed for an adequately powered

analysis not only of opioid use during pregnancy but also the sub-types of opioid use. Furthermore, the longitudinal nature of the database allows researchers to follow participants over time so long as they maintain continuous health insurance coverage. In the current research, women were followed for the duration of their pregnancy, delivery of a livebirth, and into the postpartum period. Finally, the MarketScan data has limited missingness and extensive data checks are performed prior to the release of the data.

Despite these strengths, there are some important limitations. The sample derived from the MarketScan database is a convenience sample, and while the database contains claims information for millions of individuals, the results of any analysis based on the database are not generalizable to other populations. Similarly, the employers and health plans that provide paid claims data to MarketScan are typically large employers, with medium and small employers underrepresented in the data. Data contained within the MarketScan database was not collected for epidemiological research but rather for financial purposes; therefore, diagnosis codes and dates may be poorly captured and subject to error. Finally, beginning in 2015 and continuing through 2017, there was a notable decrease in the number of individuals captured in the database. Researchers speculate that this decrease is due to more individuals obtaining health insurance via the health insurance marketplace, established by the Patient Protection and Affordable Care Act, and away from employee-sponsored health insurance. Although these limitations reduce generalizability, the population captured in the MarketScan database represents a significant portion of the privately insured population in the US and provides an opportunity to examine rare events and subpopulations among this group.

3.5 Study Population

Aim I Analytic Cohort

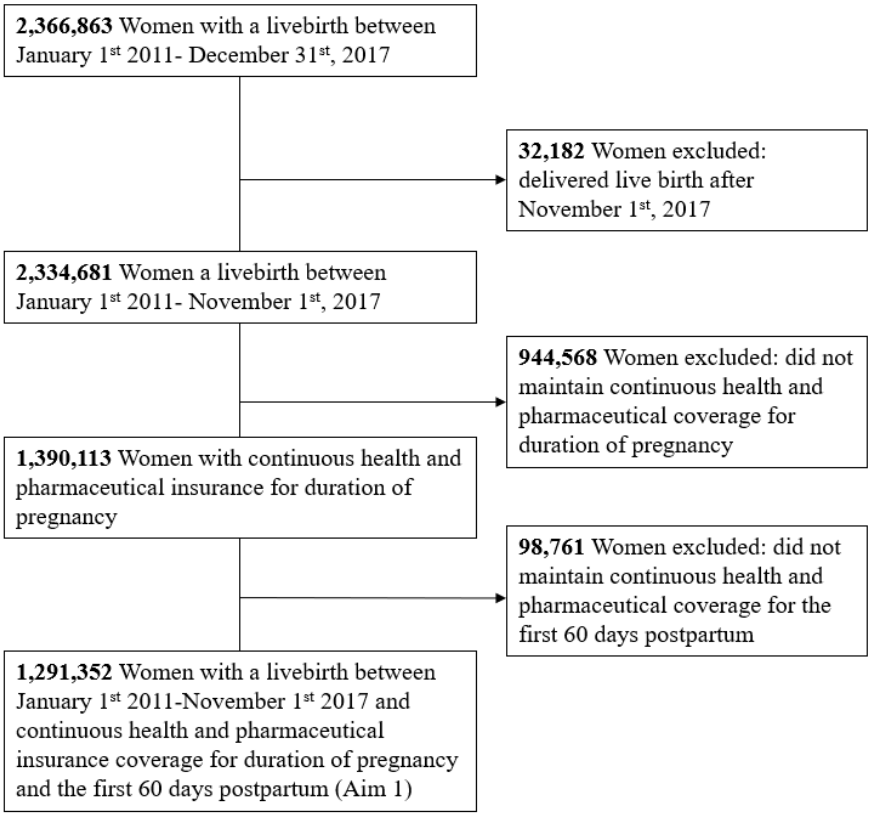
The Aim 1 analytic cohort included women with a livebirth between January 1st, 2011 and November 1st, 2017 who maintained continuous health and pharmaceutical insurance coverage for the duration of pregnancy and through the first 60 days postpartum. The 60-day timeframe coincides with the ACOG recommended guidance for the time by which women should receive contraceptive care and is in accordance with the National Quality Forum (NQF) postpartum contraceptive care performance measures [2, 3]. Length of continuous health insurance enrollment was determined after identifying the initial cohort of women with a live birth. The method for assigning the start of pregnancy was developed specifically for use with administrative databases in prior literature [4-6]. Women were eligible for inclusion in the Aim 1 analytic cohort if they maintained continuous health and pharmaceutical insurance coverage for the duration of pregnancy, defined as the 273 days prior to delivery, and for at least 60 day postpartum. The timeframe for deliveries was restricted to January 2011 through November 1st, 2017. Due to the requirement that women maintain continuous health and pharmaceutical coverage for the first 60 days postpartum, women who delivered after November 1, 2017 were not eligible for Aim 1 because they could not be observed for the first 60 days postpartum based on the available MarketScan data.

The continuous enrollment inclusion criterion was designed to increase the capture of relevant pre-existing conditions, maternal morbidities, and was crucial for identifying women who use opioids during pregnancy. Pharmaceutical claims data was used not only to identify women who used opioids during pregnancy but also identify postpartum prescription contraception that was otherwise not captured in outpatient or inpatient claims data. The

criterion that women have continuous enrollment for the first 60 days postpartum was designed to identify postpartum contraception use, the primary outcome of interest, without excluding an unnecessarily large number of women. This approach is particularly important because women who use opioids during pregnancy may have shorter continuous enrollment periods; therefore, the continuous enrollment criteria were designed to maximize both the sample size and capture of postpartum contraception while minimizing potential bias. Data that go beyond the first 60 days postpartum were included in the analysis for research Aim 2. Figure 3.1 shows the process of identifying the analytic sample for Aim 1.

An initial cohort of 2,366,863 women with a livebirth between January 2011 and December 2017 was identified. Women who delivered after November 1st, 2017 were excluded (n=32,182) followed by women who did not maintain continuous health and pharmaceutical coverage for the duration of pregnancy (n=944,568). Finally, 98,761 women who did not maintain continuous health and pharmaceutical coverage for the first 60 days postpartum were excluded, resulting in a final sample of 1,291,352 women for inclusion in the Aim 1 analysis (Figure 3.1). Once all Aim 1 inclusion criteria were satisfied; inpatient, outpatient, and outpatient pharmaceutical claims occurring in the 273 days prior to the day of delivery and for the first 60 days postpartum were included in the analytic data. The inclusion criteria were applied to the first (index) delivery for women with more than one delivery captured in the data.

Figure 3.1. Aim 1 Analytic Sample Identification



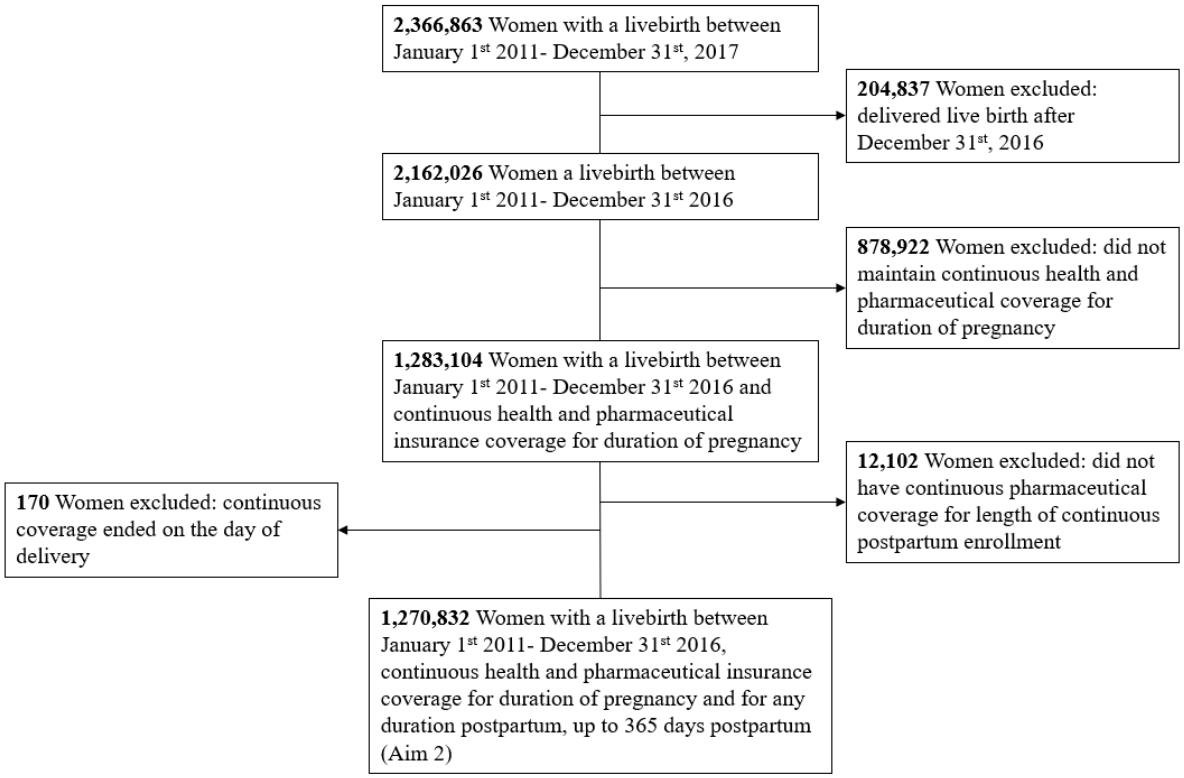
Aim 2 Analytic Cohort

The analytic cohort for Aim 2 included all women with a livebirth between January 2011 and December 2016 who maintained continuous health and pharmaceutical coverage for the duration of pregnancy and for some duration during the postpartum period, up to 365 days after delivery. No requirements were placed on length of continuous coverage during the postpartum period because Aim 2 was a time-to-event analysis, with the unit of measurement being days since delivery. However, women whose continuous coverage ended on the day of delivery were excluded (n=170) as there was no measurable time-at-risk. All data from the day of delivery onward was included in the Aim 2 analysis up until the participant experienced the event of interest (provision of prescription contraception), lost continuous coverage, or was administratively censored at 365 days postpartum. Women who delivered after December 2016

were excluded from the Aim 2 analysis in order to minimize bias due to differential follow up periods as they could not be followed for 365 days after delivery. As with Aim 1, all criteria were applied to the first live birth during the study period for each woman; higher order births to the same woman were excluded.

The Aim 2 cohort began with the identification of 2,366,863 women with a livebirth between January 2011 and December 2017. All women delivering after December 2016 were immediately excluded (n=204,837). A further 878,922 women were excluded because they did not maintain continuous health and pharmaceutical coverage for the duration of pregnancy. Finally, women who did not maintain continuous pharmaceutical coverage for the duration of their continuous postpartum health insurance enrollment were excluded (n=12,102), along with the 170 women whose continuous coverage ended on the day of delivery. The final Aim 2 analytic sample included 1,270,832 women with a livebirth between January 2011 and December 2016, who maintained continuous health and pharmaceutical insurance coverage for the duration of pregnancy and for any duration during the postpartum period, up to 365 days postpartum (see Figure 3.2). Once all Aim 2 inclusion criteria were satisfied, inpatient, outpatient, and outpatient pharmaceutical claims occurring in the 273 days prior to the day of delivery and through the first 365 days postpartum or until loss of continuous postpartum coverage, were included in the analytic data.

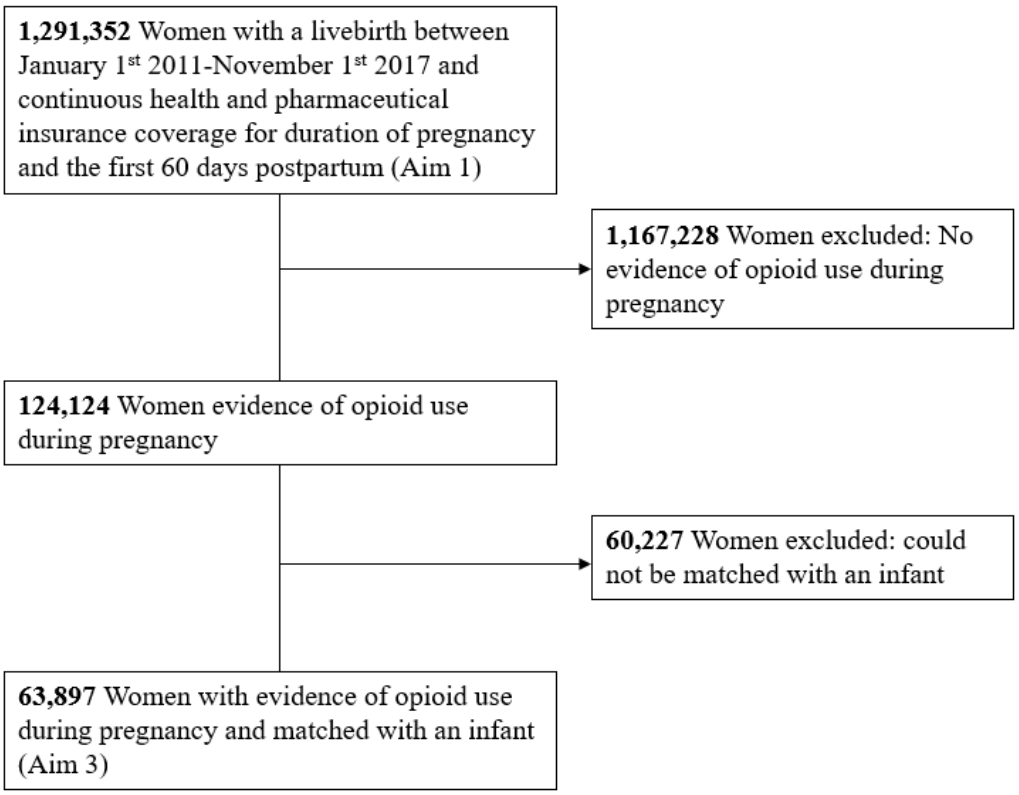
Figure 3.2. Aim 2 Analytic Sample Identification



Aim 3 Analytic Cohort

The inclusion criteria for the Aim 3 analytic cohort were the same as those for Aim 1, with the additional criteria of limiting the sample to women with evidence of opioid use during pregnancy who were matched with a liveborn infant. The Aim 3 cohort began with all women included in the Aim 1 analysis (n=1,291,352). Women with no evidence of opioid use during pregnancy were excluded (n=1,167,228) leaving 124,124 women with evidence of opioid use during pregnancy who also maintained health and pharmaceutical insurance coverage for the duration of pregnancy and for at least the first 60 days postpartum. Among the women with evidence of opioid use during pregnancy, 51.5% were successfully linked with a liveborn infant for a total sample of 63,897 women included in the Aim 3 analysis (see Figure 3.3).

Figure 3.3. Aim 3 Analytic Sample Identification



3.6 Key Measures and Variables

Obstetric Deliveries

Women were identified for inclusion in the study sample based on a delivery of a live born infant between January 2011 and December 2017 using inpatient admissions claims. For purposes of this research, the index delivery was defined as the first delivery captured during the study period; if a woman had multiple deliveries during the study time period, the exclusion criteria were only applied to the first delivery and higher order births to the same woman were excluded in order to avoid potential selection bias.

Inclusion criteria were only applied to the first livebirth because randomly selecting which livebirth to apply the inclusion criteria may have biased the sample towards women with

longer periods of continuous insurance coverage or older women as parity and age are highly correlated. The alternative approach of including multiple births to the same woman in the analytic cohort presented similar issues related to bias. The likelihood of capturing a second or higher order livebirth increases as the length of continuous insurance coverage increases. Therefore, if multiple births per woman were included in the analytic cohort, this approach would favor women with longer periods of continuous coverage and would not accurately reflect the birthing patterns within the cohort. Furthermore, women with longer periods of continuous coverage may be substantively different than women who have shorter periods of continuous health insurance coverage across demographic and clinical characteristics. This source of potential bias was eliminated by including only the first livebirth per woman captured during the study period.

The identification of index deliveries was done using validated methodology designed for insurance claims data and originally proposed by Kuklina et al. [7]. This method employs a hierarchical design for identifying deliveries using the following algorithm: (1) outcome of delivery (ICD-9-CM code = V27; ICD-10-CM code = Z370), (2) normal delivery (ICD-9-CM code = 650; ICD-10-CM Code = O80), (3) diagnosis-related group (DRG) delivery codes, and 4) ICD-9-PCS/ICD-10-PCS procedure codes for selected delivery-related procedures (see Table 3.2 for full listing of ICD-9/10 codes).

This hierarchical method was designed under the hypothesis that previous methods, which typically rely solely on the ICD-9-CM code for outcome of delivery ("V27"), did not fully capture births with acute complications. The authors applied the revised methodology to the Nationwide Inpatient Sample and demonstrated that the enhanced method captured 3.4% more obstetric deliveries than the standard methodology [7]. Importantly, the authors noted that

deliveries with acute complications such as major puerperal infections, sepsis, and respiratory distress syndrome had significantly greater odds of being missed by the standard methodology [7]. This omission is significant for this research because women who use opioids during pregnancy may experience more obstetric and fetal complications than women who do not use opioids during pregnancy, and accordingly, may be missed by using a single delivery code [8]. Furthermore, experiencing a high-risk or medically complex pregnancy may influence postpartum contraceptive method type either because of contraindications for specific methods or a strong preference to avoid a rapid repeat pregnancy [9, 10].

The Kuklina et al. algorithm was applied to the inpatient admissions data. After the initial application of the algorithm, 2,652,781 records were identified between January 2011 and December 2017 as obstetric deliveries. Records with missing enrollment IDs (n=1,232) and records to women outside of the age range of 14-55 (n=2,720) were excluded. Several approaches were employed to correctly identify the index delivery record when two or more delivery records were identified for the same woman. If two delivery records for the same woman were more than 300 days, only the first record was retained as the first record was assumed to be the first live birth captured the database (n=264,872).

The hierarchical nature of the Kuklina et al algorithm was leveraged to parse delivery records to the same woman that were less than 300 days apart. Deliveries identified by the level I code (e.g. outcome of delivery as identified by ICD- 9 code V27/ICD-10 code Z37.0), were given priority over a separate delivery claim to the same women identified by the presence of a level II-IV code. Overall, when multiple delivery records were found for a woman with less than 300 days between admissions, priority was given to the delivery record identified with the highest-level code, with level I codes being the highest. In total, 16,879 delivery records were

eliminated using this approach. Finally, any remaining unresolved delivery claim conflicts were examined on a case-by-case basis by the author, which occurred in <0.01% of identified delivery records (430 total records reviewed; 215 records dropped). The final initial cohort of deliveries included 2,366,863 women with livebirths, prior to the application of any exclusion criteria.

Table 3.2. Index Delivery Identification Algorithm from Kuklina et al.

Description	**Code Type**	**Codes**
Level I		
Outcome of Delivery	ICD-9-CM ICD-10-CM	V27 Z370
Level II		
Normal Delivery	ICD-9-CM ICD-10-CM	650 O80
Level III		
Complicated Cesarean Section	DRG	765
Uncomplicated Cesarean Section	DRG	766
Complicated Vaginal Delivery	DRG	774
Uncomplicated Vaginal Delivery	DRG	775
Uncomplicated vaginal delivery with sterilization and/or dilatation & curettage	DRG	767
Vaginal delivery with operation room procedure except sterilization and/or dilatation & curettage	DRG	768
Level IV: Selected Delivery-Related Procedures		
Forceps	ICD-9-PCS ICD-10-PCS	720, 721, 7221, 7229, 7231, 7239, 724, 726 10D07Z3, 0W8NXZZ, 10D07Z4, 10D07Z5, 10S07ZZ
Breech Extraction	ICD-9-PCS ICD-10-PCS	7251, 7252, 7253, 7254 10D07Z3, 10D07Z4, 10D07Z5, 10D07Z6
Vacuum Extraction	ICD-9-PCS ICD-10-PCS	7271, 7279 0W8NXZZ, 10D07Z6
Other specified and unspecified delivery	ICD-9-PCS ICD-10-PCS	728, 729 10D07Z8
Internal and combined version and extraction	ICD-9-PCS ICD-10-PCS	7322 10D07Z7
Other manually assisted deliveries	ICD-9-PCS ICD-10-PCS	7359 10E0XZZ
Episiotomy	ICD-9-PCS ICD-10-PCS	736 0W8NXZZ

Description	Code Type	Codes
Cesarean Section	ICD-9-PCS ICD-10-PCS	740, 741, 742, 744, 7499 10D00Z0, 10D00Z1, 10D00Z2
Exclusionary Diagnosis and Procedure Codes		
Hydatidiform Mole	ICD-9-CM ICD-10-CM	630 O01*, O08*
Abnormal Products of Conception	ICD-9-CM ICD-10-CM	631 O02*, O07* O08*
Ectopic Pregnancy	ICD-9-CM ICD-10-CM	633 O00*, O03*, O08*
Abortion	ICD-9-CM ICD-10-CM	632, 634, 635, 636, 637, 638, 639, 6901, 6951, 7491, 750 Z332, O04*, O07*, 10A07ZZ, 10A08ZZ, 10A00ZZ, 10A03ZZ, 10A04ZZ, 10A07ZX
Stillbirths	ICD-9-CM ICD-10-CM	V271, V274, V277 Z371, Z374, Z377

Postpartum Prescription Contraceptive Provision

The primary dependent variable for Aims 1-3 was provision of postpartum prescription contraception, defined and identified using NQF recommended measures and associated clinical codes [3]. The provision of postpartum prescription contraception was defined two ways, the first as a binary measure of any evidence of postpartum prescription contraception provision compared with no evidence of provision. The second measure was a categorical variable defined as no evidence of provision, moderately effective methods (MEM), long-acting reversible contraceptive methods (LARCs), and female sterilization. As proposed by the NQF measures, moderately effective contraceptive methods include the pill, patch, ring, DMPA injection, and the diaphragm. LARCs include the IUD and contraceptive implants.

Evidence of postpartum prescription contraception provision was identified using national drug codes (NDC), International Classification of Disease 9th and 10th Edition codes (ICD-9, ICD-10), Current Procedural Terminology (CPT) codes, and the Healthcare Common

Procedure Coding System (HCPCS) codes (See Table 3.3 for full list of contraceptive codes). These codes were identified and compiled by the CDC and included in the NQF recommended measure [3]. Using the codes included in the NQF recommended measure, prescription forms of contraception were identified by searching for contraceptive codes in outpatient pharmaceutical claims, inpatient admissions claims, and outpatient services claims from the date of delivery and for the duration of the postpartum period. The MarketScan database does not capture inpatient pharmaceutical claims data, therefore, contraception prescribed on an inpatient basis was not captured.

Beginning with outpatient pharmaceutical claims for the years 2011 through 2017, National Drug Codes were used to identify pharmaceutical claims associated with IUDs, contraceptive implants, DMPA injections, contraceptive pills, patch, ring, or diaphragms at any time on or after the date of delivery. Once all contraceptive claims were identified, claims with an improbable days' supply were excluded (days' supply ≤ 0 or >365). Of the 4,636,085 contraceptive claim records from 2011 through 2017, 8,509 (0.18%) had a days' supply ≤ 0; 28 records had a days' supply exceeding 365 days. Identification of contraceptive claims in inpatient admissions and outpatient services relied on ICD-9 and ICD-10, CPT, and HCPCS codes and included codes for female sterilization. If claims with a shared service date and method type for the same woman were identified across all three claim types, only the first of these duplicate records were retained. Among inpatient admissions claims for contraception, 98.0% of originally identified claims were associated with female sterilization, with very few instances of multiple claims to the same woman; therefore, no adjustments were made prior to combining these claims with other two claim types.

Once contraceptive claims were identified across all three claim types, they were combined into a single file in order to identify the postpartum contraceptive claim most proximate to the date of delivery as well as to cross-reference claims in the event that a woman had conflicting methods claims (e.g. an inpatient admissions claim for female sterilization followed by an outpatient services claim for an IUD). Several systematic methods were employed to identify the first instance of contraceptive provision following delivery. When the first contraceptive claim following delivery (or at the time of delivery) contained both a diagnosis and procedure code for sterilization or LARC, they were retained as the first postpartum provision of contraception. If all contraceptive records for a woman were outpatient prescription claims for the pill, patch, or ring, the first prescription claim was retained as the first postpartum provision of contraception. Finally, if a woman had a claim for both a LARC and moderately effective method (pill, patch, ring, DMPA, diaphragm) on the same day, the LARC method was retained.

For Aim 1, the binary and categorical measures of postpartum prescription contraceptive provision were calculated at three and 60 days postpartum, consistent with the recommended NQF measures and in alignment with clinically significant time points in the postpartum period. In Aim 3, a similar approach was taken but because of the smaller sample size, only postpartum contraceptive provision at 60 days was examined. A survival analysis approach was used in Aim 2 to examine differences in time to first contraceptive uptake, with provision of any postpartum prescription contraceptive method considered an "event".

Table 3.3 Clinical Codes Used to Identify Postpartum Contraception, Based on NQF Recommended Measures

Contraceptive Method	Clinical Codes	Data Source
Female Sterilization	ICD-9: V25.2, V26.51, 662.1, 662.2, 662.9, 663.2	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.2, Z98.51, 0UL.74ZZ, 0UL.78ZZ, 0U5.74ZZ, 0U5.78ZZ, 0UL.74DZ, 0UL.78DZ, 0UL.74CZ, 0UL.70ZZ, 0UL.73ZZ 0UL.77ZZ, 0UL.70CZ, 0UL.70DZ, 0UL.73CZ, 0UL.73DZ, 0UL.77DZ, 0UL.78DZ	
	CPT: 58600, 58605, 58615, 58611, 58670, 58671, 58565	
	HCPCS: A4264	
IUD	ICD-9: V25.11, V25.13, V25.42, V45.51, 996.32, 697	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.430, Z30.433, Z30.431, Z97.5, T83.39XA, 0UH.97HZ, 0UH.98HZ, 0UH.C7HZ, 0UH.C8HZ	
	CPT: 58300	
	HCPCS: J7300, J7301, J7302, S4989, Q0090, S4981	
	NDC: 50419042101, 50419042201, 5128520401	Outpatient Pharmaceutical Claims
Hormonal Implant	ICD-9: V25.5, V25.43, V45.52	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.49, Z30.18	
	CPT: 11981, 11983	
	HCPCS: J7306, J7307	
	NDC: 00052027201, 00052027401, 00052433001	Outpatient Pharmaceutical Claims
DMPA Injection	HCPCS: J1050, J1055	Outpatient Services Claims Inpatient Admissions Claims
	NDC: 54569370100, 54569490400, 54569552700, 54569561600, 54569621900, 54868361300, 54868410000, 54868410001, 54868525700, 55045350501, 59762453701, 59762453702, 59762453801, 59762453802, 59762453809	Outpatient Pharmaceutical Claims
Pills	ICD-9: V25.01, V25.41	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.011, Z30.41	
	HCPCS: S4993	
	NDC: 00008111720, 00008111730, 00008251402, 00008253505, 00008253601, 00008253605, 00052026106, 00052028306, 00062125100, 00062125115, 00062125120, 00062133220, 00062141116, 00062141123, 00062171400,	Outpatient Pharmaceutical Claims

Contraceptive Method	Clinical Codes	Data Source
	00062171415, 00062176100, 00062176115, 00062178100, 00062178115, 00062179600, 00062179615, 00062190120, 00062190320, 000190700, 00062190715, 00062191000, 00062191015, 00247052028, 00247069028, 00247069128, 00247069228, 00247139828, 00247151328, 00247151628, 00247151728, 00247176404, 00247176421, 00247176521, 00247198621, 00247198628, 00247200828, 00247201004, 00247201008, 00247201028, 00247201228, 00247201328, 00247214728, 00247216928, 00247217028, 00247223028, 00247223528, 00247226028, 00247226828, 00378655053, 00378727253, 00378729253, 00430042014, 00430048214, 00430053014, 00430053550, 00430057014, 00430057045, 00430058014, 00430058045, 00430058114, 00430058514, 00430058545, 00555034458, 00555071558, 00555900867, 00555900942, 00555901058, 00555901258, 00555901467, 00555901658, 00555901858, 00555902058, 00555902542, 00555902557, 00555902658, 00555902742, 00555902757, 00555902858, 00555903270, 00555903458, 00555904358, 00555904558, 00555904758, 00555904958, 00555905058, 00555905158, 00555905167, 00555906458, 00555906467, 00555906558, 00555906658, 00555906667, 00555912366, 00555913167, 00555913179, 00603359017, 00603359049, 00603752117, 00603752149, 00603752517, 00603752549, 00603754017, 00603754049, 00603760615, 00603760648, 00603760715, 00603760748, 00603760817, 00603760917, 00603762517, 00603762549, 00603763417, 00603763449, 00603764017, 00603764217, 00603766317, 00603766517, 23490765301, 23490767001, 23490769901, 24090080184, 24090096184, 35356001468, 35356001568, 35356002168, 35356025528, 35356037028, 43386062030, 45802084054, 50419040201, 50419040203, 50419040303, 50419040503, 50419040701, 50419040703, 50419041112, 50419041128, 50419043306, 50419043312, 50452025115, 50458017115, 50458017615, 50458017815, 50458019115, 50458019411, 50458019416, 50458019615, 50458019715, 50458025115, 51285005866, 51285007997, 51285008070, 51285008198, 51285008297, 51285008370, 51285008498, 51285008787, 51285009158, 51285009287, 51285011458, 51285043165, 51285054628, 51285076993, 51285094288, 51285094388, 52544014331, 52544017572, 52544020431, 52544021028, 52544021928, 52544022829, 52544023528, 52544023531, 52544024531, 52544024728, 52544024828, 52544025428, 52544025928, 52544025988, 52544026528, 52544026531, 52544026829, 52544026884, 52544027428, 52544027431,	

Contraceptive Method	Clinical Codes	Data Source
	52544027536, 52544027928, 52544028754, 52544029128, 52544029231, 52544029241, 52544029528, 52544038328, 52544038428, 52544047536, 52544055028, 52544055228, 52544055428, 52544062928, 52544063028, 52544063128, 52544084728, 52544084828, 52544089228, 52544093628, 52544094028, 52544094928, 52544095021, 52544095121, 52544095328, 52544095428, 52544095931, 52544096691, 52544096728, 52544098131, 52544098231, 52959045002, 54569067900, 54569068500, 54569068501, 54569068900, 54569068901, 54569143900, 54569384400, 54569422200, 54569422201, 54569426900, 54569427301, 54569481700, 54569487800, 54569487801, 54569489000, 54569498400, 54569499700, 54569499800, 54569516100, 54569534300, 54569534900, 54569549300, 54569549302, 54569579600, 54569579700, 54569579800, 54569581600, 54569582600, 54569603200, 54569612800, 54569614400, 54569614500, 54569627200, 54569628000, 54569628100, 54868042800, 54868044300, 54868050200, 54868050700, 54868050801, 54868050901, 54868051600, 54868151200, 54868156400, 54868231600, 54868260600, 54868270100, 54868377200, 54868386300, 54868394800, 54868409300, 54868423900, 54868436900, 54868453800, 54868459000, 54868460700, 54868473000, 54868473100, 54868474200, 54868474500, 54868475400, 54868477600, 54868481400, 54868482800, 54868485100, 54868486000, 54868491100, 54868502800, 54868528600, 54868532600, 54868535600, 54868582600, 54868582800, 54868594200, 55045283902, 55045348506, 55045349701, 55045349801, 55045378106, 55045378206, 55045378302, 55289024708, 55289088704, 55887005228, 55887028628, 58016474701, 58016482701, 66993061128, 66993061528, 68180084313, 68180084413, 68180084613, 68180084813, 68180085413, 68180087611, 68180087613, 68180089713, 68180089813, 68180090213, 68462030329, 68462030529, 68462030929, 68462031629, 68462031829, 68462038829, 68462039429, 68462055629, 68462056529	
Patch	HCPCS: J7304	Outpatient Services Claims Inpatient Admissions Claims
	NDC: 00062192001, 00062192015, 00062192024, 50458019201, 50458019215, 54569541300, 54868467000	Outpatient Pharmaceutical Claims

Contraceptive Method	Clinical Codes	Data Source
Ring	HCPCS: J7303	Outpatient Services Claims Inpatient Admissions Claims
	NDC: 00052027301, 00052027303, 54569586500, 54868483201, 55887075401	Outpatient Pharmaceutical Claims
Diaphragm	CPT: 57170 HCPCS: A4266	Outpatient Services Claims Inpatient Admissions Claims
	NDC: 00027013160, 00027013180, 00062330100, 00062330200, 00062330300, 00062330400, 00062330500, 00062330600, 00062330700, 00062330800, 00062330900, 00062331000, 00062331100, 00062331200, 00062331300, 00062334100, 00062334200, 00062334300, 00062334400, 00062334500, 00062334600, 00062334700, 00062334800, 00062334900, 00062335000, 00062335100, 00062335200, 00062338100, 00062338200, 00062338300, 00062338400, 00062338500, 00062338600, 00062338700, 00062338800, 00062338900, 00062364103, 00062364300, 00234005100, 00234013100, 00234013150, 00234013155, 00234013160, 00234013165, 00234013170, 00234013175, 00234013180, 00234013185, 00234013190, 00234013195, 00234013600, 00234013660, 00234013665, 00234013670, 00234013675, 00234013680, 00234013685, 00234013690, 00234013695, 00396401065, 00396401070, 00396401075, 00396401080	Outpatient Pharmaceutical Claims

Primary Independent Variable: Opioid Use During Pregnancy

The primary independent variable of opioid use during pregnancy was examined as a categorical variable with four mutually exclusive categories: no opioid use during pregnancy, non-chronic prescription opioid use, chronic prescription opioid use, and OUD diagnosis or Buprenorphine prescription during pregnancy (OUD/Buprenorphine category). Women with multiple forms of opioid use during pregnancy were assigned to the highest degree of opioid use indicated (from lowest to highest degree of use: non-chronic opioid use, chronic opioid use,

OUD/Buprenorphine). For instance, if a woman had an OUD diagnosis during pregnancy as well as a claim for prescription opioids (chronic or non-chronic use), she was assigned to the OUD/Buprenorphine category.

Women who used opioids during pregnancy were identified using a multipronged methodology. This approach accounts for the many forms opioid use during pregnancy can take as well as the variable time points during pregnancy and delivery when opioid use may be identified. Women were classified as having used opioids during pregnancy if any of the following diagnostic, procedure, or prescription codes were present over the course of their pregnancy: diagnosis of OUD, prescription for medication assisted therapy (MAT) (i.e. buprenorphine, excluding transdermal buprenorphine, or naltrexone), chronic prescription opioid use based on definitions used in prior literature, or non-chronic prescription opioid use [6, 11, 12]. A diagnosis of OUD was identified using ICD-9/ICD-10 codes present during any outpatient or inpatient encounter during pregnancy or at the time of delivery. The codes are consistent with prior literature as well as ACOG recommended coding for substance use during pregnancy and the postpartum period [13-16].

Women being treated for OUD with MAT were identified using outpatient pharmaceutical claims containing prescriptions for buprenorphine and naltrexone. However, because naltrexone is not approved for use in pregnant women, it is not commonly provided as a first line treatment for OUD in pregnant women [17]. Both buprenorphine and naltrexone prescriptions were identified using National Drug Codes (NDC). These codes, along with the NCD's for other prescription opiates, were obtained from a publicly available list of all opioids and opioid replacement therapy drugs currently available on the market [18] compiled by the CDC and National Center for Injury Prevention and Control. Although methadone is also

commonly used to treat OUD during pregnancy, ongoing restrictions involving the administration and prescribing of methadone to treat OUD meant it is not captured in private claims data.

Prior studies indicate that approximately 50-60% of pregnant women with OUD receive MAT in the form of methadone or buprenorphine; however, these studies are largely confined to Medicaid populations or women enrolled in clinical trials [19-21]. The results of a study evaluating MAT use among pregnant women diagnosed with OUD based on Pennsylvania Medicaid claims from 2009-2015 indicated that 27.1% of women received buprenorphine and 28.8% received methadone. Over the study period, buprenorphine use increased significantly from 15.8% in 2009 to 30.9% in 2015, with a concurrent, but smaller decline in methadone [20]. While there is no published data regarding the type of medication or trends in MAT among the privately insured pregnant population, the trend towards increased use of Buprenorphine since 2009 observed in Medicaid populations is likely reflected in the privately insured population as well.

Several studies have identified chronic or persistent opioid use during pregnancy using insurance claims data [6, 11, 22-24]. Using these studies as a guide, chronic prescription opioid use during pregnancy was defined as 30 or more days of cumulative prescription opioid availability during pregnancy by summing across all filled prescriptions, under the assumption that multiple prescriptions filled on the same date were taken concurrently [6, 11]. Opioid prescriptions, except those for buprenorphine or naltrexone, that occurred on the day of delivery were excluded as these are likely associated with cesarean delivery or other postpartum pain control and would not be considered opioid use during pregnancy. The following prescription opioids were considered when identifying chronic prescription opioid use during pregnancy:

hydrocodone, codeine, dihydrocodeine, levorphanol, nalbuphine, opioid alkaloids, oxycodone, propoxyphene, tramadol, meperidine, hydromorphone, morphine, fentanyl, butorphanol, methadone, pentazocine, tapentadol, and oxymorphone [23, 25].

The NDC's used to identify each type of opioid were obtained from the CDC and National Center for Injury Prevention and Control [18]. Methadone, for the treatment of OUD, is rarely captured in pharmaceutical insurance claims, but it is occasionally prescribed as an analgesic in patients who do not have OUD; therefore, prescription claims for methadone were used for identifying women with non-chronic and chronic prescription opioid use [25]. Non-chronic prescription opioid users during pregnancy were defined as women who filled an opioid prescription during pregnancy but did not meet the duration criteria for chronic opioid use. Prescription records with an improbable number of pills dispensed (>1,000) or days of supply (>180 days or ≤0 days) were excluded as they are likely in error; this approach is consistent with previous studies [23, 26]. In total, 1,221 prescription opioid claims records (0.4%) were dropped because of improbable days' supply.

Co-Morbidities During Pregnancy

Based on prior research, several morbidities were identified for inclusion in this research [5, 6, 13, 27-29]. These morbidities include pain-related conditions as well as common pre-existing and pregnancy-associated conditions. These comorbidities were selected to adjust for the a priori hypothesis that women with chronic and non-chronic prescription opioid use during pregnancy are also more likely to experience co-morbidities during pregnancy, particularly co-morbidities associated with pain. Furthermore, experiencing comorbidities during pregnancy is also related to postpartum contraception, particularly method type. Therefore, the inclusion of these co-morbidities strengthens the results and conclusions drawn from this analysis by

adjusting for the potential confounding effects of these co-morbidities on the association between opioid use during pregnancy and provision of postpartum prescription contraception.

Pain-related conditions included lower back pain, headache, fibromyalgia, arthritis, and neuropathic pain. These pain conditions and the associated diagnostic codes were identified by a group of researchers and clinicians at the Johns Hopkins School of Public Health who specialize in chronic pain and opioid prescribing [30]. Inclusion of these conditions is consistent with findings from the literature documenting the most common maternal conditions for which opioids may be prescribed during pregnancy [5, 6, 28, 29]. Both inpatient admissions and outpatient services claims were searched for the ICD-9-CM and ICD-10-CM codes associated with each pain-condition. A woman was considered to have a pain-related condition if two or more outpatient diagnosis codes or one or more inpatient diagnosis codes for any included condition was present during her pregnancy or at the time of delivery.

The other significant pre-existing and pregnancy-associated conditions included in the analysis were chronic hypertension, gestational hypertension, including pre-eclampsia and eclampsia, diabetes mellitus, gestational diabetes, asthma, and autoimmune disorders. Each condition was included in the models as a binary variable. Women were considered to have a pre-existing or pregnancy-associated condition if one of the associated ICD-9-CM or ICD-10-CM diagnostic codes was observed in an outpatient or inpatient record during pregnancy or at the time of delivery. These conditions are some of the most common co-morbidities among pregnant women in the US and have been included in prior research examining similar populations [13, 27]. The presence of co-morbidities during pregnancy can influence both opioid prescribing and postpartum contraception, particularly method type. Prior studies demonstrate that women with comorbidities such as chronic hypertension, diabetes, and pain

conditions are more likely to use opioids during pregnancy [6, 31]. Study results have also found that women with medically complex or high-risk pregnancies are more likely to choose sterilization or LARC for postpartum contraception than women with low-risk pregnancies [10]. There are also important contraindications for some methods of contraception in the postpartum period. Women with hypertension or those at high risk for venous thromboembolism should not use combined hormonal contraception in the postpartum period [9]. Hepatitis C was also included in descriptive tables as women who use opioid during pregnancy are known to experience significantly higher rates of hepatitis C infection during pregnancy [32].

Maternal Psychiatric Diagnosis

Maternal psychiatric conditions are an important covariable as psychiatric disorders and substance use in women are highly correlated [29, 33, 34]. Pre-existing psychiatric conditions are also associated with contraceptive method type, with women with psychiatric conditions more likely to use highly effective forms of contraception such as LARCs or sterilization [33, 35]. For this research, psychiatric conditions included major depressive disorder, bipolar disorder, schizophrenia, post-traumatic stress disorder, and generalized anxiety disorder. Based on prior literature, a woman was considered to have a psychiatric condition if two or more outpatient diagnosis codes or one or more inpatient diagnosis codes for any psychiatric condition was present during her pregnancy or at the time of delivery [14, 33, 36]. The full list of ICD-9 and ICD-10 diagnostic codes can be found in Appendix A.

Non-Opioid Substance Use Disorder

Non-opioid substance use disorders (SUDs) during pregnancy or at the time of delivery included diagnoses related to cocaine, cannabis, amphetamine, hallucinogen, alcohol, and other

substance dependence or use. Non-opioid SUDs were identified using outpatient services and inpatient admissions claims data. A woman was considered to have a non-opioid SUD if any non-opioid SUD diagnostic codes was present on an outpatient services or inpatient admissions claim during pregnancy or at the time of delivery. The full range of ICD-9 and ICD-10 diagnostic codes used to identify non-opioid SUDs during pregnancy are noted in Appendix A.

Antenatal Care

An antenatal care (ANC) visit indicator was defined as any professional claim taking place between the LMP date and the delivery date at a medical office or outpatient hospital location (place of service =11 or 22) with one of the following specialists: obstetrics & gynecology, certified nurse midwife, gynecologist, family practice, family practice OB/Gyn, certified nurse midwife, maternal and fetal medicine, nurse practitioner, or perinatology [37]. These specialists were identified using a provider type code in the MarketScan database. The ANC variable was a binary measure of any ANC verses no indication of ANC. This binary definition, rather than the timing of a first visit, was necessary because a common timeframe for pregnancy was applied to each woman. By applying a standard length of pregnancy (273 days), a more nuanced measure of ANC, such as measuring ANC by the trimester of initiation, would be inaccurate and correlated with preterm birth because women who delivered preterm would appear to have initiated ANC later in pregnancy.

Postpartum Care Visit

The variable indicating whether a woman had a postpartum care visit within the first 60 day postpartum was identified using methods previously established in the literature [14, 37]. Prior research indicates that when a woman has a routine postpartum care visit, her odds of using

a prescription form of postpartum contraception increases by 50% [38]. For this research, a woman was considered to have a postpartum care visit if she had an outpatient services claim within 60 days of delivery and if the visit took place in a medical office or outpatient hospital location (place of service code "11" or "22") and either included a postpartum care diagnosis code (ICD-9 codes: V24.1, V24.2/ICD-10 codes: Z39.1, Z.39.2) or the service provider was a specialist in one of the following: obstetrics & gynecology, certified nurse midwife, gynecologist, family practice, family practice OB/Gyn, certified nurse midwife, maternal and fetal medicine, nurse practitioner, or perinatology [37].

Infant Variables

Infant related variables, including NICU admission, NAS diagnosis, and hospital length of stay, were extracted from the inpatient admissions and inpatient services claims data associated with the infant delivery. These variables were used for the Aim 3 analysis. The revenue codes "0174" and "0175" in the inpatient services claims data were used to identify infants admitted to the NICU and a binary, yes/no variable was created based on the presence or absence of the codes. NAS diagnosis in the infant was identify using select ICD-9/ICD-10 diagnosis codes previously validated in the literature [19, 39]. A 2019 study examined the positive predictive value (PPV) of the following ICD-9/ICD-10 codes in administrative data for identifying clinically confirmed NAS cases: 779.5, 760.72 (ICD-9), P96.1, P04.49 (ICD-10) and reported a positive predictive value of 91% and 98% for the associated ICD-9 and ICD-10 codes, respectively [39].

Once an infant was identified with a diagnosis of NAS, further refinement was done by eliminating infants with probable iatrogenic NAS. Iatrogenically-induced NAS is fundamentally different from NAS caused by antenatal exposure to opioids because iatrogenic NAS is induced

by opioid analgesics provided to the infant while under clinical management during an inpatient admission; therefore, it was crucial to correctly categorize type of NAS diagnosis. Because iatrogenically-induced NAS does not have a unique diagnosis code, previously identified clinical diagnosis codes associated with iatrogenically-induced NAS were used to identify probable cases, as in prior research [40]. Infants were considered to have iatrogenic NAS if they also had a diagnosis of very low birthweight (IDC-9/ICD-10 codes V21.31, V21.32/P07.00, P07.02, P07.01, P07.03), intraventricular hemorrhage (ICD 9/ICD-10 codes 772.10, 772.12, 772.14, 772.11, 772.13/P52.3, P52.1, P52.22, P52.0, P52.21), periventricular leukomalacia (ICD 9/ICD-10 codes 779.7/P91.2), necrotizing enterocolitis (ICD 9/ICD-10 codes 777.51, 777.52, 777.53, 777.50/P77.9, P77.3, P77.2, P77.1), spontaneous intestinal perforation (ICD 9/ICD-10 codes 777.6/P78.0), or bronchopulmonary dysplasia (ICD 9/ICD-10 codes 770.7/P27.0, P27.1, P27.8) [40]. Of the initial 860 NAS diagnoses, only 8 (>0.1%) were classified as probable iatrogenic NAS. The remaining 852 cases were considered to have NAS due to antenatal opioid exposure. NAS diagnosis in the infant was a binary variable in the Aim 3 analyses and was used to explore whether opioid-related sequalae in the infant affected postpartum contraception provision among women who use opioids during pregnancy.

The final infant variable in the Aim 3 analysis was length of hospital stay, as measured in days. This variable was taken directly from the inpatient admission records associated with the infant's birth. It was measured as both a continuous variable and a binary measure of a length of stay of seven days or longer. In order to retain the maximum amount of detail concerning the impact of hospital length of stay on postpartum prescription contraception, the continuous measure of hospital length of stay was used in the adjusted Aim 3 models.

Demographic Variables

All remaining covariates including demographic and clinical variables were extracted from the delivery record. The mode of delivery was coded as a binary variable, whether a woman delivered vaginally or via cesarean-section. It was identified using ICD-9/10 diagnosis and procedure codes, used previously in the literature, that were present in the inpatient admission claims data at the time of delivery (See Appendix A) [41, 42].

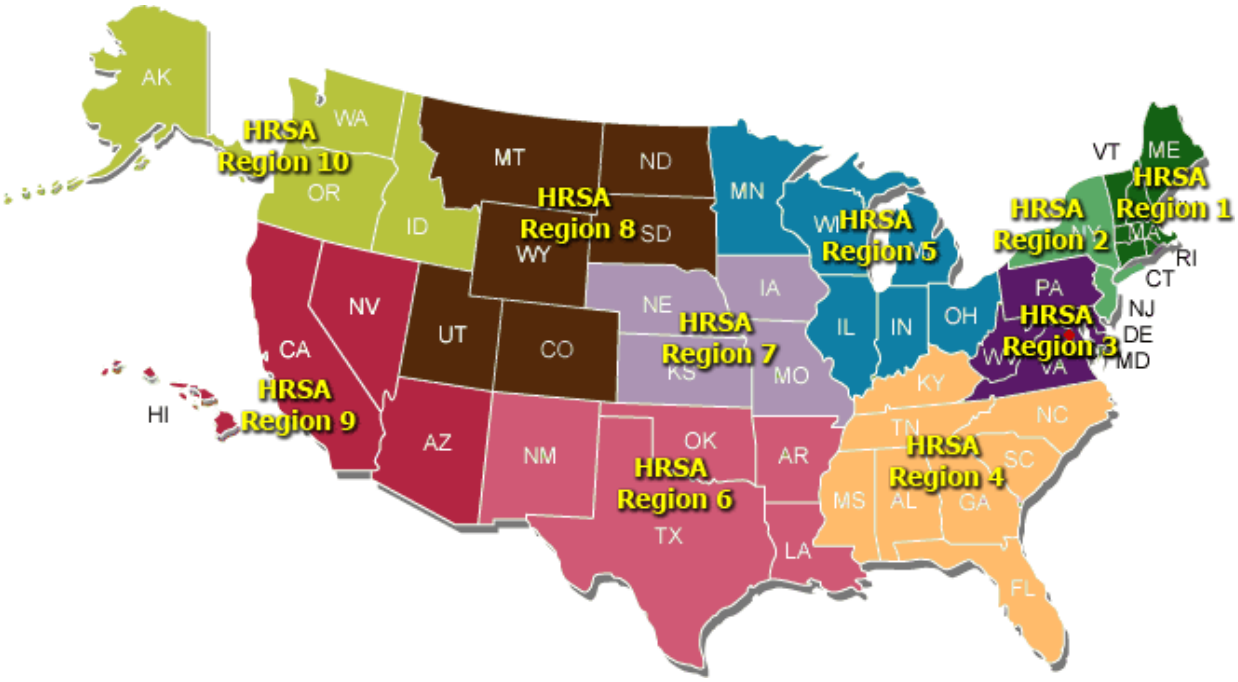
Several other variables were obtained from the delivery record, including maternal age at delivery, insurance plan type, year of delivery, and state of delivery. Maternal age at delivery was coded as a categorical variable, with categories for <20, 20-24, 25-29, 30-34, 35-40, and 40 years or older. Insurance plan type was defined based on the health insurance plan type at the time of delivery. The categories included: comprehensive, preferred provider organization (PPO), HMO and EPO, Point-of-Service (including capitation), consumer-driven health plan (CDHP), and high deductible health plans (HDHP). Type of insurance plan was included based on the hypothesis that women with more health needs, including those with substance use disorders or other chronic conditions, may choose more expansive insurance coverage, such as comprehensive plans. Furthermore, insurance plans with more comprehensive coverage may increase contraceptive uptake if woman face fewer financial and administrative obstacles to obtaining postpartum contraception. Insurance plan type had a low level of missingness (~3.0% in Aims 1-3). Rather than exclude these observations, a sixth category for "unknown insurance plan type" was included in the plan type variable. Indicator variables were included for the year of delivery (2011-2017) in order to account for secular trends in opioid use and medical practice, such as increasing postpartum LARC provision over the study period. Finally, the state in which the delivery took place was used to generate several geographic and demographic indicator variables.

The MarketScan data includes limited demographic variables except for those noted above; accordingly, state of delivery was used to create additional measures to characterize the study cohort. A region variable, modeled on the ten regions designated by the Health Resources and Services Administration (HRSA), was created based on the state in which the delivery took place (see Figure 3.4). The states grouped into each region share demographic and clinical characteristics, particularly in relation to provision and access to medical care. Prior literature has documented significant regional differences in opioid use during pregnancy, contraceptive provision overall and by method type, maternal demographic characteristics, and obstetric practices, making these geographic groupings an important adjustment variable [43-49]. A small percentage of observations (~3.0%) were missing state-level information and were placed in an "unknown" category but still included in all analyses. The MarketScan database also includes a region variable based on one of five Census regions: Northeast, North Central, South, West, and Unknown. This variable was explored in conjunction with the HRSA region variable as the HRSA regions provide more detail, but the Census regions allow for a more parsimonious model.

Beyond the HRSA and Census regional variables, demographic information including measures related to the racial composition, female educational attainment, and household income for the state in which the delivery took place were also included in the model. Indicator variables were defined as "1" if a state had the characteristic of interest and a "0", otherwise. The state-level characteristics were: 20% or more of the population identified as Hispanic; 20% or more of the population identified as Black; 15% or more of the population lived below the poverty threshold as defined by the US Census Bureau [50]; and 35% or more of females aged 18 and older have a college degree or higher (Table 3.4). For example, for a delivery taking

place in Mississippi, the state-level indicator variable for Black race and high poverty, take a value of "1" within the model. All state-level demographic data estimates were obtained from the 2013-2017 American Community Survey 5-Year Estimates [51].

Figure 3.4 Map of HRSA Regions



Source: Health Resources and Services Administration.

Table 3.4 States Included in State-Level Demographics Indicator Variables

Indicator Variable	States Meeting Indicator Variable Criteria
States in which 20% or more of the population identifies as Hispanic	Arizona, California, Colorado, Florida, Nevada, New Jersey, New Mexico, Puerto Rico, Texas
States in which 20% or more of the population identifies as Black	Alabama, Delaware, District of Columbia (D.C.), Georgia, Louisiana, Maryland, Mississippi, North Carolina, South Carolina
States in which 15% or more of the population lives at or below the poverty threshold	Alabama, Arkansas, District of Columbia (D.C.), Kentucky, Louisiana, Mississippi, New Mexico, Oklahoma, Puerto Rico, South Carolina, Tennessee, West Virginia
States in which 35% or more of women, aged 18 and older, have college degrees or higher	District of Columbia (D.C.), Massachusetts, Maryland, Colorado, Vermont, Connecticut, New Jersey, Virginia

3.7 Cohort Creation & Analytic Sample

Once the index delivery records were identified, date of delivery was assumed to be the date of admission for delivery plus one day. From there, the start date of the last menstrual period (LMP) was estimated as 273 days prior to the date of delivery. For the postpartum period, the immediate postpartum timeframe was calculated by adding three days to the date of delivery, and the second postpartum period by adding 60 days to the date of delivery. These timeframes (LMP to delivery, delivery through the postpartum period) established the time period for which continuous enrollment was required for Aims 1 and 3 and served as the timeframe for restricting the relevant claims data. The relevant time period for Aim 2 extended to a maximum of 365 days postpartum. The inpatient admissions claim associated with the index delivery and the calculated pregnancy and postpartum dates were retained in a single, master file referred to as the "index delivery file". The index delivery file was used as the building block for the creation of the analytic cohorts.

With the relevant timeframe for each index delivery established, the next step in creating the cohort involved running all appropriate diagnostic, procedure, and drug codes associated with each described variable in the respective claims data (see Table 3.1 for more detail). Claims that occurred prior to the start of pregnancy or after the specified postpartum period were excluded. After identifying all the relevant claims during the appropriate time period, an indicator variable or an otherwise simplified value for each variable was merged back into the master index delivery file, signifying whether a woman experienced the variable of interest during pregnancy, delivery, or in the postpartum period, respectively.

Information regarding postpartum contraception was integrated into the data for the cohort using several variables. First, simple indicators of any evidence of contraceptive provision during the 3-day postpartum period, 60-day postpartum period, and 365-day postpartum period were integrated. Secondly, variables reflecting the type of contraception were included. The date of the first instance of contraceptive provision within the first 365 days postpartum was included as this variable was necessary for the Aim 2 analysis. In the Aim 3 analysis, infant variables were merged into the analytic cohort file for women who were successfully linked with an infant and had evidence of opioid use during pregnancy. The final variable merged into the index delivery file was annual enrollment information. All index deliveries, regardless of meeting the continuous enrollment criteria were retained for sensitivity analyses. Indicator variables were used to denote women who maintained continuous coverage for the duration of pregnancy and for at least the first 60-days postpartum. Table 3.5 provides a listing of all covariates for Aims 1-3, as well as their associated coding. All variables reaching statistical significance of $p \leq 0.05$ in the bivariate analyses or those thought to be confounders or important predictors of postpartum contraception were included in the adjusted models.

Table 3.5 Covariates and Coding by Research Aim

Aim	Variable	Values
1, 3	*Any postpartum prescription contraceptive Provision within 60 days postpartum (outcome)*	No provision (ref.) Provision
1	*Any postpartum prescription contraceptive Provision within 60 days postpartum, by method type (outcome)*	No provision (ref.) Sterilization LARC MEM
2	*Any postpartum prescription contraceptive Provision within 365 days postpartum (outcome)*	No provision (ref.) Provision
1, 2	*Opioid use during pregnancy*	No Use (ref.) Non-chronic prescription use Chronic prescription use OUD/Buprenorphine

Aim	Variable	Values
3	*Opioid use during pregnancy*	Non-chronic prescription use (ref.) Chronic prescription use OUD/Buprenorphine
1, 2, 3	*Maternal age at delivery*	<20 20-24 25-29 (ref.) 30-34 35-39 40+
1, 2, 3	*Mode of delivery*	Vaginal (ref.) Cesarean
1, 3	*Year of delivery*	Indicator variable for 2011-2017
2	*Year of delivery*	Indicator variable for 2011-2016
1, 2, 3	*HRSA Region*	10 Region categories Region 3 (ref.)
1, 2, 3	*State of delivery: 20% or more Hispanic*	No (ref.) Gave birth in state meeting criteria
1, 2, 3	*State of delivery: 20% or more Black*	No (ref.) Gave birth in state meeting criteria
1, 2, 3	*State of delivery: 15% or more living in poverty*	No (ref.) Gave birth in state meeting criteria
1, 2, 3	*State of delivery: 35% or more of females with college or higher education*	No (ref.) Gave birth in state meeting criteria
1, 2, 3	*Insurance Plan Type*	PPO (ref.) Comprehensive HMO/EPO POS/POS+Capitation CDHP HDHP Unknown
1, 2, 3	*Non-Opioid Substance Use Disorder*	No (ref.) Yes
1, 2, 3	*Psychiatric Conditions*	No (ref.) Yes
1, 2, 3	*Pain Conditions*	No (ref.) Yes
1, 2, 3	*Chronic Hypertension*	No (ref.) Yes

Aim	Variable	Values
1, 2, 3	*Gestational Hypertension*	No (ref.) Yes
1, 2, 3	*Diabetes Mellitus*	No (ref.) Yes
1, 2, 3	*Gestational Diabetes*	No (ref.) Yes
1, 2, 3	*Asthma*	No (ref.) Yes
1, 2, 3	*Autoimmune Disorder*	No (ref.) Yes
1, 2, 3	*Hepatitis C*	No (ref.) Yes
1, 2, 3	*Any ANC*	No Yes (ref.)
1, 3	*Postpartum clinical visit within 60 days*	No visit (ref.) Visit
3	*Infant NAS diagnosis*	No (ref.) Yes
3	*Infant NICU admission*	No (ref.) Yes
3	*Infant hospital length of stay*	Continuous measure (days)

3.8 Data Analysis

Aim 1: Methods for Data Analysis

Aim 1 evaluated the association between type of opioid use during pregnancy and postpartum prescription contraceptive provision, both overall and by contraceptive method-type at 60 days postpartum. The Aim 1 cohort included women with a livebirth with continuous health and pharmaceutical insurance coverage for the duration of pregnancy and through the first 60 days postpartum. Descriptive analyses were conducted to summarize the distribution of characteristics in the study cohort, both overall and stratified by opioid use and type as well an contraceptive method. Next, unadjusted and adjusted multivariable and multinomial logistic regression models were used to assess the relationship between opioid use during pregnancy and prescription contraception provision at 60 days postpartum.

Analysis began by examining the distribution of all variables in the Aim 1 cohort, including the distribution of maternal age at delivery, year of delivery, HRSA region, state-level demographic characteristics, insurance plan type, mode of delivery, type of opioid use during pregnancy, psychiatric conditions, non-opioid substance use disorders, pain conditions, chronic hypertension, gestational hypertension, diabetes mellitus, gestational diabetes, asthma, autoimmune disorders, hepatitis C, any ANC, and postpartum clinical visit within 60 days postpartum. The descriptive analyses also included examining the Aim 1 cohort by provision of contraception at 60 days postpartum, at three days postpartum, stratified by opioid use status during pregnancy and the covariates. These descriptive analyses helped illuminate important differences within the cohort by type of contraceptive method and by type of opioid use during pregnancy. Significant changes in trends over time for the number of livebirths and provision of prescription contraception were assessed using the "nptrend" command in Stata, which performs a nonparametric test for trend across ordered groups. In this instance, the ordered groups are the years included in the study period (2011-2017).

Next, bivariate logistic regression analyses were conducted to evaluate the unadjusted relationship between contraception provision and select covariates. The variables included in the bivariate analyses were: maternal age at delivery, year of delivery, HRSA region, state-level demographic characteristics, insurance plan type, mode of delivery, type of opioid use during pregnancy, psychiatric conditions, non-opioid substance use disorders, pain conditions, chronic hypertension, gestational hypertension, diabetes mellitus, gestational diabetes, asthma, autoimmune disorders, hepatitis C, any ANC, and postpartum clinical visit within 60 days postpartum (Table 3.5).

Based on the results of the bivariate analyses and a priori hypotheses, a multivariable logistic model was fit to evaluate the adjusted odds ratios and 95% confidence intervals for the association between opioid use during pregnancy and postpartum contraceptive provision. An example is shown below of the multivariable model and interpretations of each component:

$$LogOdds(Y_i) = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \cdots + \beta_K X_{ki}$$

Where:

$LogOdds(Y_i)$= log odds of provision of any postpartum prescription contraception within 60 days following delivery for the i^{th} woman

β_0= log odds of postpartum contraceptive provision for a woman with all covariates set to 0

X_{1i} = type of opioid use during pregnancy for the i^{th} woman

β_1= change in log odds of provision of postpartum contraception use within 60 days following delivery given her category of opioid use during pregnancy for the i^{th} woman

$X_{2i} \ldots X_{ki}$ = value of covariates for the i^{th} woman

$\beta_{2 \ldots} \beta_k$ = change in log odds of the provision of postpartum contraception within 60 days following delivery for a one-unit increase in a given covariate value

A similar analysis, using a multinomial logistic regression model, was conducted for evaluating differences in the relative risk ratio (RRR) of provision of each type of contraceptive method relative to no provision. This analysis examined differences in the RRR of sterilization, LARC, or MEM, relative to no provision of a prescription contraceptive method. Contraceptive method-type grouping was based on the NQF recommended measures with moderately effective methods consisting of the pill, patch, ring, DMPA, and diaphragm and LARCs consisting of the IUD, and implant [3]. The base category for the multinomial model outcome was "no provision of a prescription method". The equations used to estimate the multinomial model are shown below, with each equation evaluating the RRR of a given contraceptive method relative to no provision of prescription contraception:

$$Ln\left(\frac{P(method = sterilization)}{P(method = none)}\right) = \beta_{10} + \beta_{11}X_{11i} + \beta_{12}X_{12i} + \cdots + \beta_{1K}X_{1ki}$$

$$Ln\left(\frac{P(method = LARC)}{P(method = none)}\right) = \beta_{20} + \beta_{21}X_{21i} + \beta_{22}X_{22i} + \cdots + \beta_{2K}X_{2ki}$$

$$Ln\left(\frac{P(method = MEM)}{P(method = none)}\right) = \beta_{30} + \beta_{31}X_{31i} + \beta_{32}X_{32i} + \cdots + \beta_{3K}X_{3ki}$$

Where:

$Ln\left(\frac{P(method=sterilization)}{P(method=none)}\right)$= relative risk ratio of sterilization within 60 days following delivery relative to no provision of prescription contraception the i^{th} woman

B_{10}= relative risk ratio of sterilization relative to no prescription contraception method within 60 days following delivery for a woman with all covariates set to 0

X_{11i} = category of opioid use during pregnancy for the i^{th} woman

β_{11}= change in relative risk ratio of sterilization relative to using no prescription contraception within three days following delivery given maternal opioid use during pregnancy for the i^{th} woman

$X_{12i}…X_{1ki}$ = value of covariates for the i^{th} woman

$\beta_{12...}\beta_{1k}$ = change in relative risk ratio of sterilization relative to using no prescription contraception within 60 days following delivery for a one-unit increase in a given covariate value

For both the multivariable logistic regression models and multinomial logistic regression models, model fit was assessed using AIC and BIC, with preference given to models with the lowest AIC and BIC [52]. All analyses were performed in Stata/MP-16 [53].

Aim 2: Methods for Data Analysis

The Aim 2 analysis examined time to first contraceptive provision within the first 365 days postpartum comparing women who did and did not use opioids during pregnancy. The analytic sample included women with a livebirth who maintained continuous health and pharmaceutical insurance coverage for the duration of pregnancy and for some period during the

postpartum, up to 365 days. Aim 2 involved a survival analysis, using Kaplan-Meier curves and Cox Proportional Hazards models.

Exploratory analyses for Aim 2 were conducted to understand the distribution of variables by contraceptive provision, including by method type, and by type of opioid use during pregnancy. Sensitivity analyses compared women included in the Aim 2 analysis with those who did not meet the inclusion criteria to identify any potential differences between the groups. Next, mean days to contraceptive provision and 95% confidence intervals were calculated for each covariate among women who received contraception within 365 days postpartum. This analysis provided a crude estimate of the mean days to contraceptive provision by type of opioid use and all other covariates. A fully adjusted analysis of mean days to contraceptive provision was also conducted by estimating the marginal means from an adjusted linear regression model. The linear regression model was adjusted for maternal age, HRSA region, state-level characteristics, insurance plan type, year of delivery, delivery mode, opioid use category, and chronic conditions. The adjusted means days to contraceptive provision and accompanying 95% confidence intervals were reported by type of opioid use.

The survival analysis began by generating Kaplan-Meier curves, including log rank tests, and log-log plots for each covariate of interest. The Kaplan-Meier curves provide a visualization of the survival function for each categorical covariate and indicate whether the groups are proportional over the study period. The log rank test, based on the Kaplan-Meier curve, is a non-parametric test of the hypothesis that the survival curves among the covariate categories are equal, with a p-value<0.05 indicating that the survival across groups is different. Log-log plots offer a similar visualization to the Kaplan-Meier curves; they are a natural log transformation of the estimated survival curve.

Bivariate Cox models were run for each covariate to assess the relationship between the covariate and risk of contraceptive provision. Covariates reaching a significance of $p<0.05$ in the univariate models or those thought to be confounders or important predictors of postpartum contraception were included in the full Cox model. Ties (e.g. two events occurring simultaneously in the data) in continuous time-to-event analyses can be problematic, therefore, Efron's approximation was used to account for possible ties in the multivariable Cox model [54]. After the full Cox model was run, the proportional hazards assumption was tested for each individual covariate based on the Schoenfeld residuals. A global test of the proportional hazards assumption was also performed. An example of the fully adjusted, Cox proportional hazards model and interpretations of each component is:

$$\lambda(t|X) = \lambda_0(t)e^{(\beta 1X1 + \beta 2X2 + \cdots + \beta pXp)}$$

Where:

$\lambda(t\|X)$ = hazard of postpartum contraceptive provision at time t for a woman with a particular set of covariate values X
$\lambda_0(t)$ = baseline hazard of postpartum contraceptive provision at time t for a woman with all covariates equal to zero
$e^{\beta 1}$ = hazard ratio of postpartum contraceptive provision comparing women who use opioids during pregnancy against those who do not, independent of time

An extensive sensitivity analysis was performed to assess the degree to which certain variables violated the proportional hazards assumption. The sensitivity analysis involved running three fully adjusted cox models across three different postpartum time periods. The first model covered the full postpartum period, delivery through 365 days postpartum and was equivalent to the full cox model presented for the final results. The second model was restricted to the date of delivery through the first 60 days postpartum and assessed the risk of failure (e.g. provision of contraception) over the first 60 days. The third model covered the timeframe of 61

days postpartum through 365 days postpartum and included women who had not experienced the outcome by 61 days postpartum and maintained continuous coverage up until that time. The severity of the violation of proportional hazards was assessed by comparing the adjusted hazard ratios across all three models. This analysis also highlighted important changes over time in the hazard of contraceptive provision over the first year postpartum.

A competing-risk model was considered for the Aim 2 analysis to account for the competing risk of a pregnancy during the postpartum period. Competing-risk in survival analysis is defined as an event that either impedes or modifies the chances of observing the event of interest, in this case, postpartum contraception provision. Experiencing a pregnancy during the postpartum period is a competing risk for postpartum contraception use as the need for contraception is eliminated if a pregnancy occurs. Only 1.15% (n=14,571) of the Aim 2 cohort had evidence of a subsequent pregnancy during the postpartum follow up period, as defined by the presence of an ANC visit. Based on the low proportion of women with evidence of a pregnancy during the postpartum period, a competing-risk model was not necessary.

Aim 3: Methods for Data Analysis

Aim 3 assessed the relationship between infant outcomes and postpartum prescription contraception provision among women with evidence of opioid use during pregnancy. The Aim 3 sample was based on women included in the Aim 1 analysis with the additional inclusion criteria of opioid use during pregnancy and successful linkage with an infant record. It was restricted to women with evidence of opioid use during pregnancy who were successfully linked with an infant record and maintained continuous health and pharmaceutical insurance coverage for the duration of pregnancy and through the first 60 days postpartum. Initial exploratory analysis was conducted comparing the distribution of characteristics between the women

successfully linked with an infant record, those who were not linked, and the full cohort of women with evidence of opioid use during pregnancy from Aim 1. This analysis served as both a sensitivity analysis and an exploration of potential differences between the two groups. Further sensitivity analysis was performed to better understand potential selection bias in the Aim 3 cohort; this analysis is explained in detail at the end of this section.

Descriptive statistics were performed for the Aim 3 cohort, including characterizing provision of contraception within 60 days postpartum by the covariates. Several exploratory analyses focused on the infant-related variables including examining type of opioid use during pregnancy by NAS status in the infant; contraceptive method provision by NAS status in the infant and by NICU admission; and average infant hospital length of stay by type of contraceptive provision. Each infant-focused descriptive analysis provided insight into how infant outcomes may relate to postpartum contraceptive provision.

Bivariate associations of the infant-related variables and covariates with contraceptive provision within 60 days postpartum were conducted using logistic regression. A fully adjusted logistic regression model was fit including all independent variables that reached a significance level of $p<0.05$ in the bivariate models and variables with a theoretical or established relationship with postpartum contraception. Model fit and selection was based on both AIC and BIC, with preference given to models with the lowest AIC and BIC [52]. An example of the fully adjusted, multivariable model and interpretations of each component is shown here:

$$LogOdds(Y_i) = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \cdots + \beta_K X_{ki}$$

Where:

$LogOdds(Y_i)$= log odds of provision of any postpartum prescription contraception within 60 days following delivery for the i^{th} woman

β_0= log odds of postpartum contraceptive provision for a woman with all covariates set to 0

X_{1i} = type of opioid use during pregnancy for the i^{th} woman

β_1= change in log odds of provision of postpartum contraception use within 60 days following delivery given her category of opioid use during pregnancy for the i^{th} woman

$X_{2i}…X_{ki}$ = value of covariates for the i^{th} woman

$\beta_{2...}\beta_k$ = change in log odds of the provision of postpartum contraception within 60 days following delivery for a one-unit increase in a given covariate value

Further exploration of potential selection bias was warranted for the Aim 3 cohort because of significant differences between the women successfully linked to an infant record compared to those who were not. This analysis involved calculating the relative odds ratio (ROR), a method used to quantify the magnitude and direction of selection bias in cohort studies [55-57]. The ROR is calculated by dividing the crude odds ratios from the subpopulation by the crude odds ratio in the source population. In this sensitivity analysis, women who used opioids during pregnancy in the Aim 1 cohort served as the source population and women included in the Aim 3 analysis were the subpopulation. The crude odds ratio used for the ROR analysis was the odds of contraceptive provision among women with OUD/Bup compared to the odds of provision among women with non-chronic prescription opioid use, as women with non-chronic prescription opioid use were the reference group in the Aim 3 analysis. An ROR equal to 1 indicates there is no differential selection bias because the ORs from the source and subpopulation are equivalent; however, an ROR>1 indicates an overestimation of the true association between the exposure and outcome of interest in the subpopulation; an ROR<1 indicates an underestimation.

Figure 3.5 Method for Calculating Relative Odds Ratio for Aim 3 Sensitivity Analysis

Opioid Use Category	Provided Contraception	Not Contraceptive Provision

OUD/Bup	a_{aim3} | A_{aim1}	b_{aim3} | B_{aim1}
Non-chronic Prescription Opioid Use	c_{aim3} | C_{aim1}	d_{aim3} | D_{aim1}

ROR Equation: $\frac{\frac{a}{A}*\frac{d}{D}}{\frac{b}{B}*\frac{c}{C}} = (a*d)/(b*c) \Big/ (A*D)/(B*C) = \frac{OR_{aim3}}{OR_{aim1}} = \text{ROR}$

3.9 Ethical Considerations

This study was exempted by the Institutional Review Board at the Johns Hopkins Bloomberg School of Public Health as it was a secondary analysis of existing de-identified data. Data access was granted by the Center for Drug Safety and Effectiveness, a joint center at the Johns Hopkins School of Public Health and Johns Hopkins School of Medicine. The Center for Drug Safety and Effectiveness maintains a paid subscription to the MarketScan Database and provides access to the database for researchers and graduate students after submission and approval of a project application. The MarketScan Database is owned, compiled, and maintained by IBM.

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Chapter 4. Study Results

4.1 Overview

This chapter describes the findings for the three study aims: Aim 1) Evaluate the association between opioid use during pregnancy and prescription contraception provision by 60 days postpartum, including by contraceptive method type; Aim 2) Evaluate the time to first prescription contraception provision during the postpartum period for women who did and did not use opioids during pregnancy, including by type of opioid; and Aim 3) Assess if adverse newborn outcomes are associated with provision of prescription contraception within 60 days postpartum among women who used opioids during pregnancy.

This chapter opens with a description of the analytic cohorts for Aims 1 and 2. Next, the aim-specific results are presented beginning with descriptive statistics specific to opioid use during pregnancy followed by descriptive statistics for contraceptive provision. Bivariate and main multivariable model results are then presented, including any sensitivity analyses. The Aim 3 results, including a description of the analytic cohort are presented at the end of the chapter, because the Aim 3 cohort was substantively different from Aims 1 and 2. The chapter closes with a brief summary of the study results.

4.2 Study Sample Characteristics

Table 4.1 shows the descriptive characteristics of the analytic cohorts for Aims 1 and 2. Across both Aims, the majority of live births were to women ages 30-34 and who lived in HRSA Region's 4 and 5 which primarily include states in the South and Midwest. Approximately 3.0% of livebirths were to women with unknown geographic region. Most women were insured through a PPO plan type. Clinically, 65% of women had a vaginal delivery and the most common comorbidity experienced during pregnancy was gestational diabetes. As anticipated, the cohorts for Aims 1 and 2 were very similar in size and distribution of covariates.

The average age of delivery was the same for Aims 1 and 2, as was the age distribution. The largest percentage of births was in Region 4, consisting of states in the South, and the overall distribution of births across HRSA region was similar for both Aims. The prevalence of comorbidities was nearly identical for Aims 1 and 2, except for pain conditions which had a slightly higher prevalence in the Aim 1 cohort (8.3% vs 7.7%). Finally, postpartum contraception provision in the Aim 2 sample was higher overall compared to Aim 1 because of the longer postpartum time period examined in Aim 2.

Table 4.1 Descriptive Characteristics of Aims 1 and 2, Column Totals

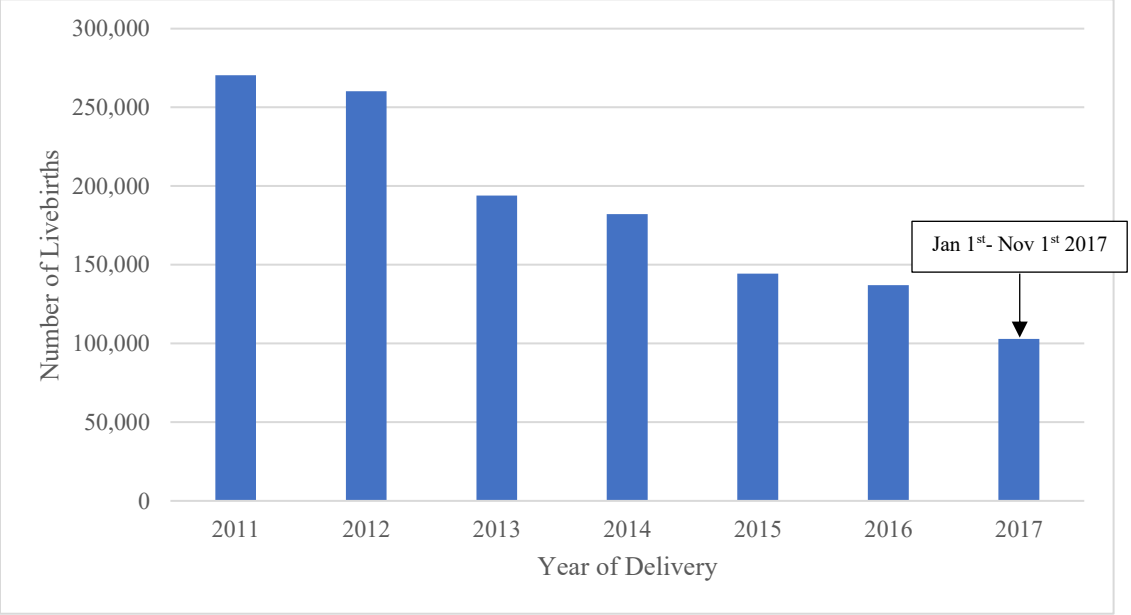
	Aim 1 Cohort	**Aim 2 Cohort**
Total N	1,291,352	1,270,832
Opioid Use During Pregnancy		
No Opioid Use	90.4% (1,167,228)	89.9% (1,142,590)
Non-Chronic Prescription Use	8.5% (109,622)	8.9% (113,273)
Chronic Prescription Use	0.7% (9,347)	0.8% (9,838)
OUD Diagnosis/Bup Prescription	0.4% (5,155)	0.4% (5,127)
Contraceptive provision within 60 Days Postpartum		N/A
No Provision	62.4% (806,103)	
Evidence of Provision	37.6% (485,249)	
Sterilization	6.1% (79,130)	
LARC	7.0% (90,391)	
Moderately Effective Methods	24.5% (315,728)	
Any contraceptive provision within 365 days of delivery	N/A	
No Provision		49.8% (632,814)
Evidence of Provision		50.2% (638,018)
Sterilization		6.6% (84,450)
LARC		11.9% (150,776)
Moderately Effective Methods		31.7% (402,792)
Age, mean years (SD)	30.3 (5.5)	30.2 (5.5)
Age, Categorical		
<20	2.9% (36,882)	2.9% (37,089)
20-24	12.3% (159,196)	12.4% (158,131)
25-29	27.6% (356,299)	27.9% (354,483)
30-34	35.3% (455,415)	35.1% (445,584)
35-39	17.6% (227,946)	17.4% (221,526)
40+	4.3% (55,614)	4.2% (54,019)
HRSA Region		
Region 1	4.3% (55,782)	4.3% (55,254)
Region 2	7.5% (97,282)	7.3% (93,385)

	Aim 1 Cohort	Aim 2 Cohort
Region 3	8.6% (111,514)	8.8% (111,322)
Region 4	21.7% (280,470)	20.9% (265,460)
Region 5	18.3% (236,920)	18.6% (236,731)
Region 6	13.2% (170,845)	13.3% (169,643)
Region 7	4.1% (52,726)	4.0% (51,232)
Region 8	3.2% (41,104)	3.2% (40,969)
Region 9	12.0% (155,183)	12.2% (154,906)
Region 10	4.0% (51,831)	3.9% (50,210)
Unknown	2.9% (37,695)	3.3% (41,720)
Delivery in State with ≥20% Hispanic Population	29.4% (380,268)	29.5% (374,670)
Delivery in State with ≥20% Black Population	16.6% (214,766)	15.9% (202,221)
Delivery in State with ≥15% Population in Poverty	13.5% (174,548)	13.1% (167,013)
Delivery in State with ≥35% Women with College Degree or More	10.1% (130,623)	10.0% (127,759)
Insurance Plan Type		
PPO	59.4% (767,515)	60.2% (764,813)
Comprehensive	1.0% (13,122)	0.9% (11,523)
HMO/EPO	14.7% (189,842)	14.9% (189,815)
POS/POS+Capitation	7.3% (94,444)	7.2% (92,110)
CDHP	8.2% (105,445)	7.5% (95,381)
HDHP	6.1% (78,302)	5.6% (71,385)
Unknown	3.3% (42,682)	3.6% (45,805)
Year of Delivery		
2011	20.9% (270,505)	22.2% (282,670)
2012	20.1% (260,183)	22.3% (283,552)
2013	15.0% (194,041)	16.2% (205,679)
2014	14.1% (182,215)	15.8% (201,057)
2015	11.2% (144,467)	11.9% (151,938)
2016	10.6% (136,978)	11.5% (145,936)
2017	8.0% (102,963)	N/A
Delivery Mode		
Vaginal	64.5% (832,323)	64.5% (819,145)
Cesarean	35.5% (459,029)	35.5% (451,687)
Non-Opioid Substance Use Disorder	1.4% (17,584)	1.3% (17,044)
Any Psychiatric Diagnoses	5.5% (71,707)	5.5% (70,309)
Chronic Hypertension	8.4% (108,503)	8.3% (105,662)
Gestational Hypertension	12.1% (156,217)	12.1% (153,854)
Diabetes Mellitus	4.2% (54,023)	4.2% (53,843)
Gestational Diabetes	14.4% (186,290)	14.7% (187,131)
Asthma	4.9% (62,718)	4.8% (60,791)
Autoimmune Disease	1.9% (24,769)	1.9% (23,925)
Pain Condition	8.3% (107,444)	7.7% (97,478)
Hepatitis C	0.07% (948)	0.07% (870)
Any ANC	96.8% (1,249,770)	96.6% (1,227,456)
Postpartum Care Visit within 60 Days	45.1% (582,078)	N/A

N/A= Not applicable; indicates a variable that was not included in the research aim

The number of livebirths that met the inclusion criteria for Aims 1 and 2 decreased steadily over the study period. The number decreased by 49% from 2011 to 2016, the last full year of births, from a high of 270,505 livebirths in 2011 to 136,978 in 2016 for the Aim 1 sample (p for trend<<0.001) (Figure 4.1). A similar downward trend in the number of livebirths was observed for Aim 2. Although researchers have not empirically confirmed the reason for the decrease, it is thought that the decline in the overall capture of the MarketScan database beginning in 2015 is due to an increasing number of people moving to the insurance exchange marketplace and away from employer-sponsored health insurance plans. The MarketScan database only includes claims to people enrolled in employer-sponsored health insurance plans. The decline in livebirths may also be explained, in part, by the ongoing decline in US fertility rates beginning in 2015 [1].

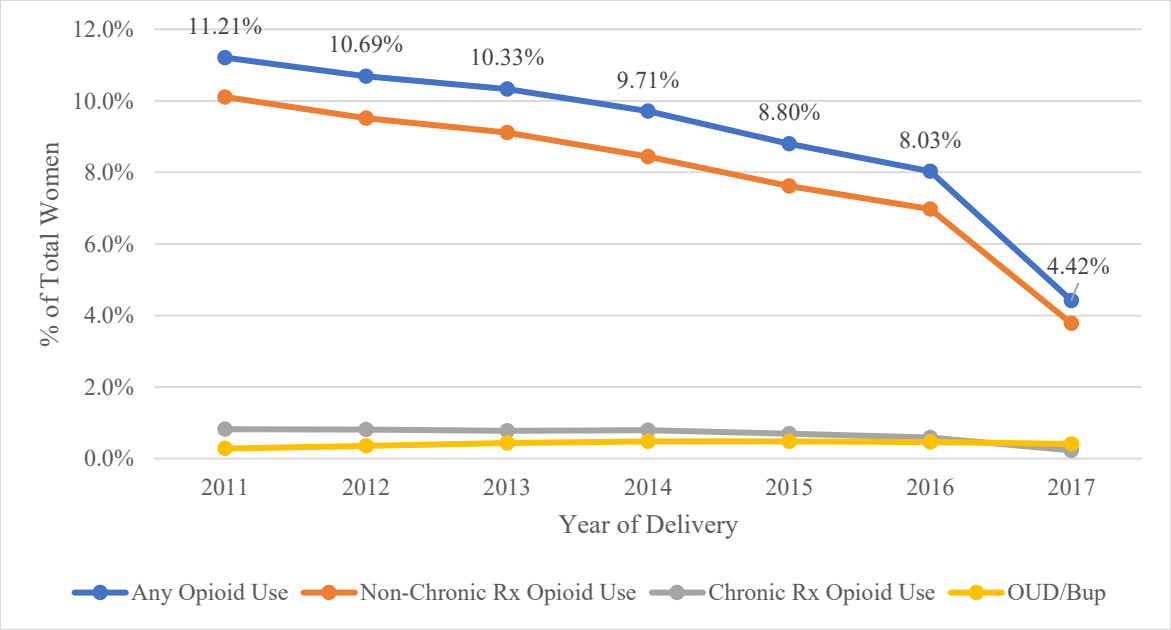
Figure 4.1 Number of Livebirths in Aim 1 Cohort by Year of Delivery, 2011-2017



4.3 Aim 1 Results

The primary independent variable in the Aim 1 analysis was opioid use during pregnancy. Overall, 90.4% of women in the Aim 1 cohort had no evidence of opioid use during pregnancy. Just over 8% of women had evidence of non-chronic prescription opioid use; 0.7% evidence of chronic prescription opioid use; and 0.4% had an OUD diagnosis or buprenorphine prescription (OUD/Bup) during pregnancy or at the time of delivery. Opioid use during pregnancy, in any form, was highest in 2011 and steadily decreased each year thereafter (p for trend<<0.001) (Figure 4.2).

Figure 4.2 Trends in Opioid Use During Pregnancy, Overall and By Opioid Type in Aim 1 Cohort



There were substantial differences in the characteristics of women by category of opioid use during pregnancy (Table 4.2). The mean age of women in the OUD/Bup group was younger compared with other categories of use, including non-use. Women in the oldest age group had the highest prevalence of chronic prescription opioid use; 1.2% of women aged 40 and older had evidence of chronic prescription opioid use compared with 0.3% for women under 20. HRSA

regions 4 and 6, comprised of states in the South and Southwest, had the highest overall levels of opioid use during pregnancy, largely due to high levels of non-chronic opioid use (>10.0%). Region 2, including New York, New Jersey, and Puerto Rico, had the lowest levels of opioid use, with just 5.6% of women having evidence of opioid use during pregnancy. Women who delivered in states where 35% or more of the female population had at least a college degree had lower levels of opioid use than the overall Aim 1 cohort (7.8% vs. 9.6%). There was little variation in opioid use during pregnancy across health insurance plan types.

Women with a cesarean delivery were somewhat more likely to use opioids during pregnancy (11.8%) than women with a vaginal birth (8.4%). Women with a non-opioid substance use disorder (SUD) were substantially more likely to use opioids across all categories of use, with a pronounced increase for chronic prescription and OUD/Bup use. Women with a psychiatric diagnosis also had higher levels of opioid use across all categories than women who did not have a diagnosis. Levels of non-chronic and chronic prescription opioid use were higher for women with all other comorbidities compared to women with no use; OUD/Bup was higher for women with pain conditions, hepatitis C, asthma, and autoimmune disorders, but similar for women with and without all other comorbidities. Women with pain-related conditions had noticeably higher levels of non-chronic prescription opioid use (15.8%) and chronic prescription opioid use (3.0%) than women without pain conditions. Women who attended a postpartum care visit within 60 days of delivery had slightly higher levels of opioid use during pregnancy compared with those with no postpartum care visit (10.8% vs. 8.7%).

Table 4.2 Characteristics of Aim 1 Cohort by Type of Opioid Use During Pregnancy, Row Totals

	No Opioid Use During Pregnancy	Non-chronic Prescription Opioid Use	Chronic Prescription Opioid Use	OUD Diagnosis or Buprenorphine Prescription
Total N (%)	1,167,228 (90.4%)	109,622 (8.5%)	9,347 (0.7%)	5,155 (0.4%)
Age, mean years (SD)	30.3 (5.4)	30.0 (5.7)	31.4 (5.6)	26.5 (5.9)
Age, Categorical				
<20	88.8% (32,748)	9.7% (3,578)	0.3% (112)	1.2% (444)
20-24	88.0% (140,106)	10.1% (16,130)	0.6% (967)	1.2% (1,993)
25-29	90.6% (322,841)	8.4% (30,012)	0.7% (2,335)	0.3% (1,111)
30-34	91.2% (415,424)	7.8% (35,752)	0.7% (3,251)	0.2% (988)
35-39	90.5% (206,260)	8.4% (19,160)	0.9% (2,018)	0.2% (508)
40+	89.6% (49,849)	9.0% (4,990)	1.2% (664)	0.2% (111)
HRSA Region				
Region 1	92.9% (51,806)	6.2% (3,475)	0.4% (247)	0.5% (254)
Region 2	94.4% (92,223)	4.7% (4,584)	0.4% (416)	0.5% (479)
Region 3	91.5% (102,007)	7.3% (8,123)	0.7% (790)	0.5% (594)
Region 4	88.7% (248,858)	10.1% (28,322)	0.8% (2,165)	0.4% (1,125)
Region 5	91.1% (215,754)	7.7% (18,373)	0.7% (1,711)	0.5% (1,082)
Region 6	88.6% (151,386)	10.3% (17,550)	0.8% (1,410)	0.3% (499)
Region 7	89.9% (47,424)	9.0% (4,766)	0.8% (400)	0.3% (136)
Region 8	90.1% (37,027)	8.8% (3,624)	0.8% (312)	0.3% (141)
Region 9	90.5% (140,390)	8.5% (13,187)	0.8% (1,188)	0.3% (418)
Region 10	90.7% (47,014)	8.0% (4,139)	0.7% (382)	0.6% (294)
Unknown Region	89.4% (33,339)	9.3% (3,479)	0.9% (324)	0.4% (133)
Delivery in State with ≥20% Hispanic Population				
Yes	90.0% (342,091)	9.0% (34,311)	0.7% (2,793)	0.3% (1,073)
No	90.6% (825,137)	8.3% (75,311)	0.7% (6,554)	0.4% (4,082)
Delivery in State with ≥20% Black Population				
Yes	88.8% (190,742)	10.0% (21,574)	0.8% (1,692)	0.3% (758)
No	90.7% (976,486)	8.2% (88,048)	0.7% (7,655)	0.4% (4,397)
Delivery in State with ≥15% Population in Poverty				
Yes	88.7% (154,804)	9.9% (17,322)	0.9% (1,511)	0.5% (911)
No	90.6% (1,012,424)	8.3% (92,300)	0.7% (7,836)	0.4% (4,244)
Delivery in State with ≥35% Women with College Degree or More				
Yes	92.2% (120,379)	6.9% (9,055)	0.5% (700)	0.4% (489)
No	90.2% (1,046,849)	8.7% (100,567)	0.7% (8,647)	0.4% (4,666)
Insurance Plan Type				
PPO	90.3% (692,755)	8.6% (65,730)	0.8% (5,904)	0.4% (3,126)
Comprehensive	88.9% (11,669)	8.8% (1,152)	1.2% (156)	1.1% (145)
HMO/EPO	89.8% (170,517)	9.1% (17,371)	0.7% (1,306)	0.3% (648)
POS/POS+Capitation	90.1% (85,070)	8.8% (8,319)	0.7% (648)	0.4% (407)
CDHP	91.0% (95,985)	8.0% (8,414)	0.6% (640)	0.4% (406)
HDHP	92.4% (72,385)	6.7% (5,289)	0.5% (393)	0.3% (235)
Unknown	91.0% (38,847)	7.8% (3,347)	0.7% (300)	0.4% (188)

	No Opioid Use During Pregnancy	Non-chronic Prescription Opioid Use	Chronic Prescription Opioid Use	OUD Diagnosis or Buprenorphine Prescription
Year of Delivery				
2011	88.8% (240,190)	10.1% (27,341)	0.8% (2,215)	0.3% (759)
2012	89.3% (232,369)	9.5% (24,760)	0.8% (2,117)	0.4% (937)
2013	89.7% (173,988)	9.1% (17,681)	0.8% (1,520)	0.4% (852)
2014	90.3% (164,520)	8.4% (15,378)	0.8% (1,446)	0.5% (871)
2015	91.2% (131,758)	7.6% (11,014)	0.7% (1,007)	0.5% (688)
2016	92.0% (125,996)	7.0% (9,555)	0.6% (802)	0.5% (625)
2017	95.6% (98,407)	3.8% (3,893)	0.2% (240)	0.4% (423)
Delivery Mode				
Vaginal	91.6% (762,463)	7.4% (61,598)	0.6% (5,005)	0.4% (3,257)
Cesarean	88.2% (404,765)	10.5% (48,024)	0.9% (4,342)	0.4% (1,898)
Non-Opioid Substance Use Disorder				
Yes	64.3% (11,299)	11.0% (1,935)	3.8% (668)	20.9% (3,682)
No	90.7% (1,155,929)	8.4% (107,687)	0.7% (8,679)	0.1% (1,473)
Psychiatric Disorder, Any				
Yes	81.9% (58,724)	13.3% (9,553)	2.5% (1,802)	2.3% (1,628)
No	90.9% (1,108,504)	8.2% (100,069)	0.6% (7,545)	0.3% (3,527)
Chronic Hypertension				
Yes	86.3% (93,620)	11.7% (12,715)	1.5% (1,647)	0.5% (521)
No	90.8% (1,073,608)	8.2% (96,907)	0.6% (7,700)	0.4% (4,634)
Gestation Hypertension				
Yes	87.3% (136,318)	11.1% (17,378)	1.2% (1,852)	0.4% (669)
No	90.8% (1,030,910)	8.1% (92,244)	0.7% (7,495)	0.4% (4,486)
Diabetes Mellitus				
Yes	87.2% (47,117)	11.1% (5,985)	1.3% (697)	0.4% (224)
No	90.5% (1,120,111)	8.4% (103,637)	0.7% (8,650)	0.4% (4,931)
Gestational Diabetes				
Yes	89.1% (165,947)	9.7% (18,097)	0.9% (1,704)	0.3% (542)
No	90.6% (1,001,281)	8.3% (91,525)	0.7% (7,643)	0.4% (4,613)
Asthma				
Yes	85.6% (53,701)	12.3% (7,745)	1.4% (861)	0.7% (411)
No	90.6% (1,113,527)	8.3% (101,877)	0.7% (8,486)	0.4% (4,744)
Autoimmune Disorder				
Yes	84.6% (20,952)	11.7% (2,899)	3.0% (739)	0.7% (179)
No	90.5% (1,146,276)	8.4% (106,723)	0.7% (8,608)	0.4% (4,976)
Hepatitis C				
Yes	58.6% (556)	8.9% (84)	1.2% (11)	31.3% (297)
No	90.4% (1,166,672)	8.5% (109,538)	0.7% (9,336)	0.4% (4,858)
Pain-Related Conditions				
Yes	80.3% (86,239)	15.8% (16,948)	3.0% (3,242)	0.9% (1,015)
No	91.3% (1,080,989)	7.8% (92,674)	0.5% (6,105)	0.3% (4,140)
Any ANC				
Yes	90.3% (1,128,888)	8.5% (106,787)	0.7% (9,090)	0.4% (5,005)

	No Opioid Use During Pregnancy	Non-chronic Prescription Opioid Use	Chronic Prescription Opioid Use	OUD Diagnosis or Buprenorphine Prescription
No	92.2% (38,340)	6.8% (2,835)	0.6% (257)	0.4% (150)
Postpartum Care Visit within 60 Days of Delivery				
Yes	89.2% (519,289)	9.4% (54,955)	0.9% (5,227)	0.5% (2,607)
No	91.3% (647,939)	7.7% (54,667)	0.6% (4,120)	0.4% (2,548)
Postpartum Contraception Use within Three days				
No evidence of provision	90.7% (1,93,024)	8.2% (98,661)	0.7% (7,979)	0.4% (4,741)
Evidence of provision	85.3% (74,204)	12.6% (10,961)	1.6% (1,368)	0.5% (414)
Female Sterilization	84.5% (61,306)	13.3% (9,691)	1.7% (1,263)	0.4% (322)
LARC	88.9% (1,184)	8.3% (111)	1.0% (14)	1.7% (22)
Moderately Effective Methods				0.5% (70)
Provided Postpartum Contraception within 60 days Postpartum				
No Evidence of Provision	91.1% (734,766)	7.8% (62,763)	0.6% (5,188)	0.4% (3,386)
Evidence of Provision	89.1% (432,462)	9.7% (46,859)	0.9% (4,159)	0.4% (1,769)
Female Sterilization	84.3% (66,706)	13.5% (10,661)	1.8% (1,408)	0.5% (355)
LARC	89.0% (80,473)	9.8% (8,822)	0.7% (682)	0.5% (409)
Moderately Effective Methods	90.4% (285,278)	8.7% (27,376)	0.7% (2,069)	0.3% (1,005)

Dependent Variable: Postpartum Prescription Contraceptive Provision

The dependent variable in Aim 1 was provision of prescription contraception within 60 days postpartum, both overall provision and by contraceptive method type. Descriptive statistics are provided for contraceptive provision within three days postpartum and 60 days postpartum in Table 4.3 for the Aim 1 cohort. Because the overall prevalence was low, only descriptive statistics are provided for provision within three days postpartum.

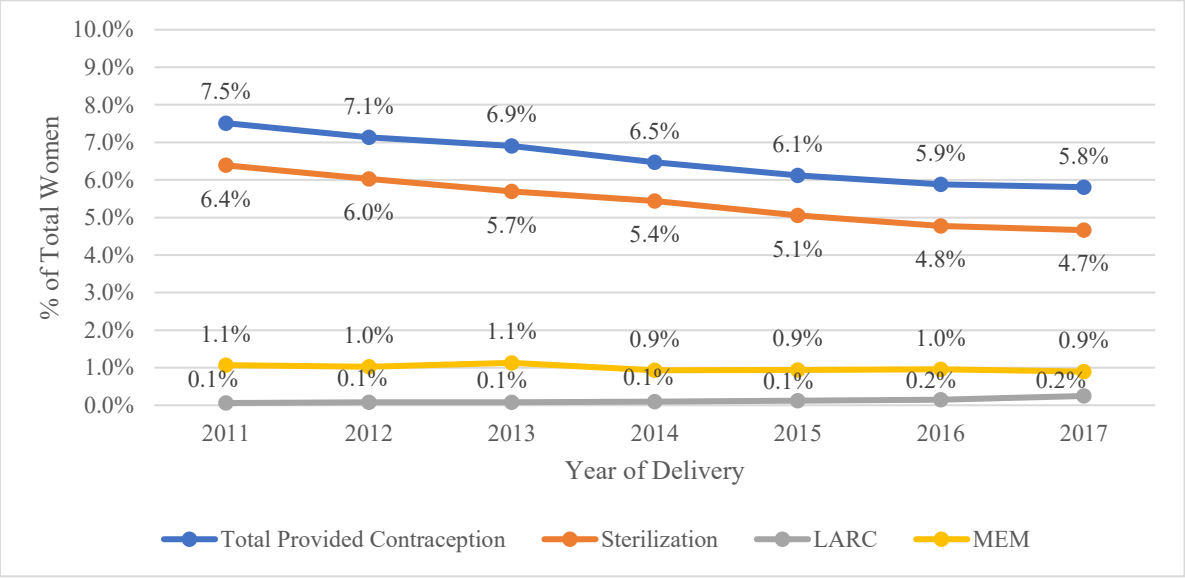
Contraceptive provision within three days postpartum was low, with just 6.7% of women receiving any prescription contraception in the immediate postpartum period (Table 4.3). Provision within three days decreased over the study period from a high of 7.5% in 2011 to 5.8% in 2017 (p for trend<0.00), with declines largely attributable to decreases in immediate

postpartum sterilization (Figure 4.3). Provision of LARC methods within three days increased over the study period but remained low, reaching a high of only 0.2% in 2017. Provision of MEM was also low, but it remained steady over the study period ranging from 1.1% in 2011 to 0.9% in 2017. Female sterilization was the most common method provided within three days postpartum, but it decreased from 6.4% in 2011 to 4.7% in 2017. Figure 4.3 shows the trends for each method over the study period. A full descriptive analysis of the provision of prescription contraception within three days postpartum can be found in Appendix B.

Table 4.3 Provision of Contraception within 3 and 60 Days Postpartum, Aim 1 Cohort

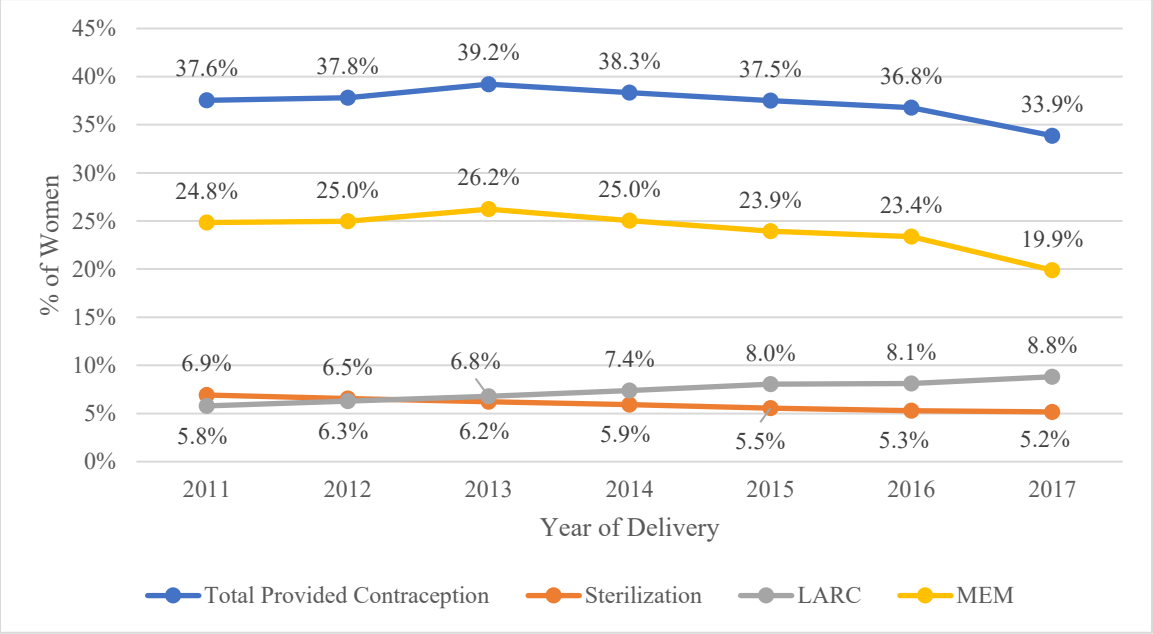
Provision of Contraception, N (%)	No Evidence of Provision	Evidence of Provision	Sterilization	LARC	Moderately Effective Methods
3-Days Postpartum	1,204,405 (93.3%)	86,947 (6.7%)	72,582 (5.6%)	1,331 (0.1%)	13,034 (1.0%)
60-Days Postpartum	806,103 (62.4%)	485,249 (37.6%)	79,130 (6.1%)	90,391 (7.0%)	315,728 (24.4%)

Figure 4.3 Trends for Provision of Prescription Contraception within 3-Days Postpartum, Overall and by Method Type, Aim 1 Cohort



Overall, 37.6% of women in the Aim 1 cohort were provided prescription contraception within 60 days postpartum (Table 4.3), with the majority receiving a MEM. Female sterilization rates declined over the study period from 6.9% in 2011 to 5.2% in 2017 (p for tend<0.00) while LARC provision increased from 5.8% to 8.8% (p for trend <0.00) (Figure 4.4). The provision of MEM was variable, ranging from a high of 26.2% in 2013 to a low of 19.9% in 2017. It is unclear why it decreased from 23.4% in 2016 to 19.9% in 2017.

Figure 4.4 Trends for Provision of Prescription Contraception within 60-Days Postpartum, Overall and by Method Type, Aim 1 Cohort



Provision of prescription contraception within 60 days postpartum as well as method type varied by several covariates (Table 4.4). There were marked differences among the various types of opioid use during pregnancy. Overall, women with chronic prescription opioid use had the highest levels of contraceptive provision and women with OUD/Bup, the lowest. Levels of sterilization were higher for each category of opioid use than for women who did not use opioids during pregnancy, with a substantially higher sterilization prevalence among women with

chronic prescription opioid use. LARC provision was also higher for all categories of opioid use compared with women who did not use opioids during pregnancy, whereas MEM provision was lower for women with chronic prescription opioid use and OUD/Bup. These same trends were reflected in the 3-day contraceptive provision measure (see Appendix B).

Women undergoing female sterilization had the highest average age (33.1 years), while women receiving LARC were the youngest (28.1 years). Women in the oldest age group (40+ years) had the lowest overall levels of contraceptive provision while women in their 20's had the highest levels. The prevalence of sterilization increased with age, whereas the provision of LARC was highest in the youngest age categories. Provision of contraception varied across HRSA regions from a low of 25.8% in Region 2 (NY, NJ, PR) to a high of 42.6% in Region 8 (MT, ND, SD, WY, UT, CO). Female sterilization was highest in the southern US (Regions 4 and 6), and LARC provision was highest in the west (Regions 8 and 10). MEM provision was consistent across regions, except for lower rates in Region 2.

Women with comorbidities had higher levels of contraceptive provision except those with autoimmune disorders and hepatitis C, as did women with cesarean deliveries, who experienced higher levels of contraceptive provision, specifically sterilization. Women who attended a postpartum care visit within 60 days postpartum had significantly higher levels of contraception provision, with a pronounced increase in levels of LARC provision.

Table 4.4 Characteristics of Aim 1 Cohort by Postpartum Contraceptive Method Provision Within 60 Days of Delivery, Row Totals

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	Moderately Effective Methods
Total N (%)	806,103 (62.4%)	485,249 (37.6%)	79,130 (6.1%)	90,391 (7.0%)	315,728 (24.4%)
Opioid Use					

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	Moderately Effective Methods
No Opioid Use During Pregnancy	62.9% (734,766)	37.0% (432,462)	5.7% (66,706)	6.9% (80,478)	24.4% (285,278)
Non-Chronic Prescription Opioid Use	57.2% (62,763)	42.7% (46,859)	9.7% (10,661)	8.0% (8,822)	25.0% (27,376)
Chronic Prescription Opioid Use	55.5% (5,188)	44.5% (4,159)	15.1% (1,408)	7.3% (682)	22.1% (2,069)
OUD Diagnosis/ Buprenorphine Prescription	65.7% (3,386)	34.3% (1,769)	6.9% (355)	7.9% (409)	19.5% (1,005)
Age, mean years (SD)	30.2 (5.5)	29.7 (5.4)	33.1 (4.9)	28.1 (5.4)	29.2 (5.0)
Age, Categorical					
<20	60.2% (22,219)	39.8% (14,663)	0.03% (12)	13.6% (5,066)	26.1% (9,645)
20-24	59.5% (94,695)	40.5% (64,501)	1.7% (2,775)	11.4% (18,232)	27.3% (43,494)
25-29	59.3% (211,435)	40.7% (144,864)	3.8% (13,584)	8.0% (28,602)	28.8% (102,678)
30-34	63.2% (287,640)	36.8% (167,775)	6.3% (28,674)	5.9% (27,052)	24.6% (112,049)
35-39	66.2% (150,929)	33.8% (77,017)	11.3% (25,758)	4.4% (9,952)	18.1% (41,307)
40+	70.5% (39,185)	29.5% (16,429)	15.0% (8,327)	2.8% (1,547)	11.8% (6,555)
HRSA Region					
Region 1	66.5% (37,093)	33.5% (18,689)	3.8% (2,121)	6.6% (3,705)	23.1% (12,863)
Region 2	74.2% (72,184)	25.8% (25,098)	4.0% (3,938)	2.7% (2,652)	19.0% (18,508)
Region 3	65.3% (72,797)	34.7% (38,717)	5.8% (6,44)	4.7% (5,240)	24.2% (27,033)
Region 4	58.2% (163,141)	41.8% (117,329)	8.1% (22,704)	7.8% (21,972)	25.9% (72,653)
Region 5	63.3% (149,905)	36.7% (87,015)	4.9% (11,741)	6.2% (14,639)	25.6% (60,635)
Region 6	58.4% (99,720)	41.6 (71,125)	8.4% (14,411)	8.2% (14,016)	25.0% (42,698)
Region 7	58.1% (30,617)	41.9% (22,109)	5.7% (3,017)	9.0% (4,738)	27.2% (14,354)
Region 8	57.3% (23,575)	42.6% (17,529)	4.7% (1,917)	13.8% (5,686)	24.1% (9,926)
Region 9	66.8% (103,62)	33.2% (51,563)	4.7% (7,376)	5.4% (8,379)	23.1% (35,808)
Region 10	58.5% (30,329)	41.5% (21,502)	5.3% (2,749)	13.0% (6,736)	23.2% (12,017)
Unknown	61.3% (23,122)	38.7% (14,573)	7.2% (2,712)	7.0% (2,628)	24.5% (9,233)
Delivery in State with ≥20% Hispanic Population					

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	Moderately Effective Methods
Yes	64.1% (243,857)	35.9% (136,411)	6.4% (24,531)	6.5% (24,914)	22.9% (86,966)
No	61.7% (562,246)	38.3% (348,838)	6.0% (54,599)	7.2% (65,477)	25.1% (228,762)
Delivery in State with ≥20% Black Population					
Yes	57.9% (124,342)	42.1% (90,424)	8.1% (17,478)	7.8% (16,780)	26.1% (56,166)
No	63.3% (681,761)	36.7% (394,825)	5.7% (61,652)	6.8% (73,611)	24.1% (259,562)
Delivery in State with ≥15% Population in Poverty					
Yes	56.0% (97,736)	36.6% (408,437)	8.5% (14,801)	7.7% (13,530)	27.8% (48,481)
No	63.4% (708,367)	44.0% (76,812)	5.8% (64,329)	6.9% (76,861)	23.9% (267,247)
Delivery in State with ≥35% Women with College Degree or More					
Yes	67.3% (87,980)	32.6% (42,643)	4.6% (5,966)	5.7% (7,439)	22.4% (29,238)
No	61.9% (718,123)	38.1% (442,606)	6.3% (73,164)	7.1% (82,952)	24.7% (286,490)
Insurance Plan Type					
PPO	62.3% (478,058)	37.7% (289,457)	6.3% (48,161)	7.0% (53,791)	24.4% (187,505)
Comprehensive	63.8% (8,378)	36.1% (4,744)	5.6% (742)	7.4% (972)	23.1% (3,030)
HMP/EPO	62.5% (118,576)	37.5% (71,266)	5.5% (10,422)	7.0% (13,282)	25.0% (47,562)
POS	62.0% (58,605)	37.9% (35,839)	6.7% (6,357)	6.8% (6,387)	24.4% (23,095)
CDHP	61.7% (65,033)	38.3% (40,412)	6.1% (6,389)	7.7% (8,139)	24.5% (25,884)
HDHP	64.8% (50,765)	35.2% (27,537)	5.2% (4,098)	7.0% (5,480)	22.9% (17,959)
Unknown	62.5% (26,688)	37.5% (15,994)	6.9% (2,961)	5.5% (2,340)	25.0% (10,693)
Year of Delivery					
2011	62.4% (168,929)	37.5% (101,576)	6.9% (18,713)	5.8% (15,650)	24.8% (67,213)
2012	62.2% (161,856)	37.8% (98,327)	6.5% (17,036)	6.3% (16,341)	24.9% (64,950)
2013	60.8% (117,953)	39.2% (76,088)	6.2% (12,043)	6.8% (13,152)	26.2% (50,893)
2014	61.7% (112,372)	38.3% (69,843)	5.9% (10,780)	7.4% (13,465)	25.0% (45,598)
2015	62,5% (90,276)	37.5% (54,191)	5.5% (8,010)	8.0% (11,612)	23.9% (34,569)
2016	63.2% (86,618)	36.8% (50,360)	5.3% (7,233)	8.1% (11,095)	23.4% (32,032)
2017	66.1% (68,099)	33.9% (34,864)	5.2% (5,315)	8.8% (9,076)	19.9% (20,473)
Delivery Mode					
Vaginal	65.4% (544,714)	34.5% (287,609)	2.0% (16,642)	7.5% (62,411)	25.1% (208,556)

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	Moderately Effective Methods
Cesarean	56.9% (261,389)	43.1% (197,640)	13.6% (62,488)	6.1% (27,980)	23.3% (107,172)
Non-Opioid SUD					
Yes	62.1% (10,919)	37.9% (6,665)	6.0% (1,050)	9.4% (1,661)	22.5% (3,954)
No	62.4% (795,184)	37.6% (478,584)	6.1% (78,080)	7.0% (88,730)	24.5% (311,774)
Psychiatric Disorder, Any					
Yes	60.5% (43,353)	39.5% (28,354)	7.0% (5,040)	8.8% (6,283)	23.7% (17,031)
No	62.5% (762,750)	37.5% (456,895)	6.1% (74,090)	6.9% (84,108)	24.5% (298,697)
Chronic Hypertension					
Yes	58.0% (62,979)	42.0% (45,524)	10.0% (10,856)	7.7% (8,309)	24.3% (26,359)
No	62.8% (743,124)	37.2% (439,725)	5.8% (68,274)	6.9% (82,082)	24.5% (289,369)
Gestational Hypertension					
Yes	59.4% (92,804)	40.6% (63,413)	7.0% (10,997)	7.7% (12,090)	25.8% (40,326)
No	62.8% (713,299)	37.2% (421,836)	6.0% (68,133)	6.9% (78,301)	24.3% (275,402)
Diabetes Mellitus					
Yes	61.6% (33,259)	38.4% (20,764)	11.6% (6,296)	5.9% (3,215)	20.8% (11,253)
No	62.5% (772,844)	37.5% (464,485)	5.9% (72,834)	7.0% (87,176)	24.6% (304,475)
Gestational Diabetes					
Yes	62.2% (115,968)	37.7% (70,322)	9.1% (17,042)	6.1% (11,371)	22.5% (41,909)
No	62.4% (690,135)	37.5% (414,927)	5.6% (62,088)	7.1% (79,020)	24.8% (273,819)
Asthma					
Yes	60.0% (37,610)	40.0% (25,108)	6.4% (4,029)	8.2% (5,127)	25.4% (15,952)
No	62.5% (768,493)	37.4% (460,141)	6.1% (75,101)	6.9% (85,264)	24.4% (299,776)
Autoimmune Disease					
Yes	63.1% (15,624)	36.9% (9,145)	7.3% (1,816)	6.7% (1668)	22.9% (5,661)
No	62.4% (790,479)	37.6% (476,104)	6.1% (77,314)	7.0% (88,723)	24.5% (310,067)
Pain Condition					
Yes	61.2% (65,714)	38.8% (41,730)	7.2% (7,762)	8.4% (9,082)	23.2% (24,886)
No	62.5% (740,389)	37.5% (443,519)	6.0% (71,368)	6.9% (81,309)	24.6% (290,842)
Hepatitis C					

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	Moderately Effective Methods
Yes	65.0% (616)	35.0% (332)	7.2% (68)	8.0% (76)	19.8% (188)
No	62.4% (805,487)	37.6% (484,917)	6.1% (79,062)	7.0% (90,315)	24.4% (315,540)
Any ANC					
Yes	62.3% (778,439)	37.7% (471,331)	6.1% (76,840)	7.0% (88,024)	24.5% (306,467)
No	66.5% (27,664)	33.5% (13,918)	5.5% (2,290)	5.7% (2,367)	22.3% (9,261)
Postpartum Care Visit within 60 Days of Delivery					
Yes	54.3% (316,214)	45.7% (265,864)	6.2% (35,943)	13.6% (79,347)	25.9% (150,574)
No	69.1% (489,889)	30.9% (219,385)	6.1% (43,187)	1.6% (11,044)	23.3% (165,154)

Aim 1: Logistic Regression Models, Unadjusted and Adjusted for Outcome 1

With a sample of over one million livebirths, most variables in the bivariate logistic regression models were significantly associated ($p<<0.001$) with receipt of any postpartum prescription contraception within 60 days postpartum. Each category of opioid use was significantly associated with receipt of any postpartum contraception compared to women who did not use opioids during pregnancy. Table 4.5 shows the unadjusted and adjusted odds of receipt of a prescription for postpartum contraception for the categories of opioid use and covariates. For the sake of brevity, only the results for the adjusted model will be discussed.

Table 4.5 Unadjusted and Adjusted Odds of Postpartum Prescription Contraceptive Provision within 60 Days Postpartum, Aim 1 (N=1,291,352)

	Unadjusted OR	Adjusted OR
Opioid Use		
No Opioid Use During Pregnancy	(ref.)	(ref.)
Non-Chronic Prescription Opioid Use	1.27 (1.25-1.28)***	1.13 (1.12-1.15)***
Chronic Prescription Opioid Use	1.36 (1.31-1.42)***	1.19 (1.14-1.24)***
OUD Diagnosis/Buprenorphine Prescription	0.89 (0.84-0.94)***	0.80 (0.75-0.85)***
Age, Categorical		
<20	0.96 (0.94-0.98)**	0.98 (0.95-1.00)*
20-24	0.99 (0.98-1.01)	0.99 (0.98-1.00)

	Unadjusted OR	Adjusted OR
25-29	(ref.)	(ref.)
30-34	0.85 (0.84-0.86)***	0.86 (0.85-0.87)***
35-39	0.74 (0.73-0.75)***	0.75 (0.74-0.76)***
40+	0.61 (0.60-0.62)***	0.60 (0.59-0.61)***
HRSA Region		
Region 1	0.95 (0.93-0.97)***	0.99 (0.97-1.01)
Region 2	0.65 (0.64-0.67)***	0.69 (0.68-0.70)***
Region 3	(ref.)	(ref.)
Region 4	1.35 (1.33-1.37)***	1.22 (1.19-1.25)***
Region 5	1.09 (1.07-1.11)***	1.02 (1.00-1.04)*
Region 6	1.34 (1.32-1.36)***	1.36 (1.33-1.40)***
Region 7	1.36 (1.33-1.39)***	1.28 (1.25-1.31)***
Region 8	1.40 (1.37-1.43)***	1.45 (1.41-1.48)***
Region 9	0.93 (0.92-0.95)***	1.05 (1.02-1.08)***
Region 10	1.33 (1.30-1.36)***	1.26 (1.24-1.29)***
Unknown	1.18 (1.16-1.21)***	1.14 (1.11-1.17)***
Delivery in State with ≥20% Hispanic Population	0.90 (0.89-0.91)***	0.86 (0.84-0.88)***
Delivery in State with ≥20% Black Population	1.25 (1.24-1.27)***	0.99 (0.98-1.01)
Delivery in State with ≥15% Population in Poverty	1.36 (1.35-1.38)***	1.11 (1.10-1.13)***
Delivery in State with ≥35% Women with College Degree or More	0.79 (0.78-0.80)***	0.96 (0.94-0.98)***
Insurance Plan Type		
PPO	(ref.)	(ref.)
Comprehensive	0.93 (0.90-0.97)***	0.92 (0.88-0.95)***
HMO/EPO	0.99 (0.98-1.00)	1.05 (0.103-1.06)***
POS/POS+Capitation	1.01 (0.99-1.02)	1.00 (0.99-1.01)
CDHP	1.03 (1.01-1.04)***	1.01 (0.99-1.02)
HDHP	0.89 (0.88-0.91)***	0.95 (0.93-0.96)***
Unknown	0.99 (0.97-1.00)	1.06 (1.04-1.09)***
Year of Delivery		
2011	1.00 (0.98-1.01)	Omitted
2012	1.01 (1.00-1.02)*	1.01 (1.00-1.03)*
2013	1.08 (1.07-1.09)***	1.09 (1.07-1.10)***
2014	1.04 (1.03-1.05)***	1.04 (1.03-1.06)***
2015	0.99 (0.98-1.00)	0.98 (0.97-0.99)**
2016	0.96 (0.95-0.97)***	0.95 (0.93-0.96)***
2017	0.84 (0.83-0.85)***	0.83 (0.81-0.84)***
Delivery Mode		
Vaginal	(ref.)	(ref.)
Cesarean	1.43 (1.42-1.44)***	1.47 (1.46-1.48)***
Non-Opioid Substance Use Disorder	1.01 (0.98-1.04)	0.97 (0.94-1.01)

	Unadjusted OR	Adjusted OR
Psychiatric Disorder, Any	1.09 (1.07-1.11)***	1.05 (1.03-1.07)***
Chronic Hypertension	1.22 (1.21-1.24)***	1.10 (1.09-1.12)***
Gestational Hypertension	1.01 (1.00-1.01)	0.98 (0.97-1.00)*
Diabetes Mellitus	1.04 (1.02-1.06)***	1.00 (0.98-1.02)
Gestational Diabetes	1.15 (1.14-1.17)***	0.97 (0.96-0.99)***
Asthma	1.11 (1.09-1.13)***	1.09 (1.07-1.11)***
Autoimmune Disease	0.97 (0.95-1.00)*	0.96 (0.94-0.99)*
Hepatitis C	0.89 (0.78-1.02)	-
Pain Condition	1.06 (1.05-1.07)***	0.99 (0.98-1.01)
Any ANC	1.20 (1.18-1.23)***	-
Postpartum Care Visit within 60 Days of Delivery	1.88 (1.86-1.89)***	1.84 (1.83-1.86)***

**p<0.05, **p<0.01, ***p<<0.001*

The fully adjusted, multivariable logistic regression model included adjustments for maternal age at delivery, HRSA region of delivery, state-level demographic characteristics, insurance plan type, year of delivery, mode of delivery, non-opioid SUD, psychiatric disorders, chronic hypertension, gestational hypertension, diabetes mellitus, gestational diabetes, asthma, autoimmune disease, pain conditions, and receipt of a postpartum care visit within 60 days of delivery. The results of the fully adjusted logistic regression model are presented in Table 4.5.

After adjustment for all covariates, the relationship between type of opioid use during pregnancy and postpartum contraceptive provision was unchanged. Women with non-chronic prescription opioid use (aOR: 1.13, 95% CI: 1.12-1.15) and chronic prescription opioid use (aOR: 1.19, 95% CI: 1.14-1.24) had significantly increased odds of receiving any postpartum prescription contraception than women who did not use opioids during pregnancy. Women with OUD/Bup had significantly decreased odds of receiving postpartum contraception compared with women who did not use opioids during pregnancy (aOR: 0.80, 95% CI: 0.75-0.85).

Several demographic variables remained significantly associated with the odds of receiving postpartum contraception in the fully adjusted model. Maternal age at the time of

delivery remained significant for the oldest women (30 years or older), who had decreased odds of receipt, with the odds decreasing as age increased, like the findings in the unadjusted model. HRSA Region of delivery was also significant, with significantly increased odds of receiving any postpartum prescription contraception for women in all Regions except 1 (ME, NH, VT, MA, RI, CT) and 2 (NY, NJ, PR) compared with the reference region (Region 3- MD, VA, PA, DE, WV). Consistent with the unadjusted results, women who delivered in states with 20% or more Hispanic population had significantly decreased odds of receiving postpartum contraception (aOR: 0.86, 95% CI: 0.84-0.88), but delivering in a state with 20% or more Black population was no longer significantly associated with receipt of postpartum contraception. Women delivering in a state with 15% or more of the population living in poverty remained significantly more likely to receive postpartum contraception. Similarly, women delivering in a state where 35% or more of the women have at least a college degree, remained significantly less likely to receive postpartum contraception although the magnitude of the relationship was attenuated in the adjusted model. The relationship between year of delivery and receipt of postpartum contraception was largely unchanged from the unadjusted model.

Women with a cesarean delivery had 1.47 (95% CI: 1.46-1.48) times the odds of receipt of postpartum contraception than women with a vaginal delivery. In addition, women who attended a postpartum care visit within 60 days of delivery had significantly increased odds of receiving postpartum contraception (aOR: 1.84, 95% CI: 1.83-1.86). Women with a psychiatric disorder (aOR: 1.05, 95% CI: 1.03-1.07), chronic hypertension (aOR: 1.10, 95% CI: 1.09-1.12), or asthma (aOR: 1.09, 95% CI: 1.07-1.10) had significantly increased odds of receiving postpartum contraception in the adjusted model. Women with gestational hypertension (aOR: 0.98, 95% CI: 0.97-1.00), gestational diabetes (aOR: 0.97, 95% CI: 0.96-0.99), or an

autoimmune disease (aOR: 0.96, 95% CI: 0.94-0.99) had decreased odds of receiving postpartum contraception. The odds of receipt of postpartum prescription contraception did not differ significantly for women with non-opioid SUD, diabetes mellitus, or pain conditions compared to women without these conditions.

Model Fit Diagnostics

Model diagnostics were assessed using the Bayesian information criteria (BIC) and Akaike information criteria (AIC), both of which assess model fit, with lower scores indicating better model fit (Table 4.6). Although commonly used to assess goodness-of-fit for logistic regression, the Hosmer-Lemeshow goodness-of-fit test is not recommended for sample sizes over 25,000. At sample sizes greater than 25,000, the Hosmer-Lemeshow goodness-of-fit test is over powered and will result in a significant p-value even with small deviations between the observed and expected probability of the outcome [2]. Therefore, the combined information from the AIC and BIC were used to select the final model. The final model was built by adding successive blocks of similar variables to the model, with each block improving the model fit.

Several variables were excluded from the fully adjusted model. Hepatitis C, although included in the descriptive tables, was excluded from the final model because of its low prevalence of <1.0% in the total sample. Women with OUD are known to have significantly higher rates of hepatitis C; it was included for descriptive purposes for this reason [3]. Similarly, the receipt of any antenatal care was also considered in the descriptive tables; because of the low percentage of the cohort with no indication of receiving antenatal care it was excluded from the models. Furthermore, because it was necessary to define ANC as “any” or “none”, it did not add substantive information to address the research question. Finally, to avoid multiple collinearity among the year of delivery dummy variables, the dummy variable for 2011 was omitted from the

fully adjusted model. All odds ratios for the year of delivery variables are interpreted relative to delivery in 2011.

Table 4.6 Aim 1 Multivariable Logistic Regression Model Fit Diagnostics

	Model Description	BIC	AIC
Model 1	Demographic variables (Maternal Age, HRSA Region, State Characteristics, Insurance Place Type, Year of Delivery)	-1.648e+07	1.309
Model 2	Model 1 + Opioid Use	-1.648e+07	1.308
Model 3	Model 2 + Chronic Conditions	-1.648e+07	1.307
Model 4 (Final)	Model 3 + Delivery Mode + PNC visit	-1.652e+07	1.279

Aim 1: Multinomial Regression Models, Unadjusted and Adjusted for Outcome 2

The second set of models in the Aim 1 analysis examined receipt of postpartum contraception within 60 days of delivery by method type using multinomial logistic regression models. The categories for these models were no evidence of provision of prescription contraception (reference), female sterilization, LARC, and MEM. The results from the unadjusted and fully adjusted multinomial models are presented as relative risk ratios (RRR) in Tables 4.7 and 4.8, respectively. For the sake of brevity, only results from the fully adjusted model are discussed below for all method types.

Table 4.7 Multinomial Results: Unadjusted Relative Risk Ratios for Provision of Contraception within 60 Days Postpartum, Relative to No Provision, by Method Type (N=1,291,352)

	Sterilization	LARC	Moderately Effective Methods
Opioid Use			
No Opioid Use During Pregnancy	(ref.)	(ref.)	(ref.)
Non-Chronic Prescription Opioid Use	1.87 (1.83-1.91)***	1.28 (1.25-1.31)***	1.12 (1.11-1.14)***
Chronic Prescription Opioid Use	2.99 (1.81-3.17)***	1.20 (1.11-1.30)***	1.03 (0.97-1.08)
OUD Diagnosis/Buprenorphine Prescription	1.15 (1.03-1.29)**	1.10 (0.99-1.22)	0.76 (0.71-0.82)***
Age, Categorical			

	Sterilization	LARC	Moderately Effective Methods
<20	0.01 (0.00-0.2)***	1.66 (1.61-1.72)***	0.89 (0.87-0.92)***
20-24	0.46 (0.44-0.47)***	1.42 (1.39-1.45)***	0.94 (0.93-0.96)***
25-29	(ref.)	(ref.)	(ref.)
30-34	1.55 (1.52-1.58)***	0.69 (0.68-0.71)***	0.80 (0.79-0.81)***
35-39	2.65 (2.60-2.71)***	0.48 (0.47-0.50)***	0.56 (0.55-0.57)***
40+	3.30 (3.21-3.41)***	0.29 (0.27-0.31)***	0.34 (0.33-0.35)***
HRSA Region			
Region 1	0.64 (0.61-0.68)***	1.39 (1.33-1.45)***	0.93 (0.91-0.96)***
Region 2	0.61 (0.59-0.64)***	0.51 (0.49-0.53) ***	0.69 (0.67-0.70)***
Region 3	(ref.)	(ref.)	(ref.)
Region 4	1.57 (1.53-1.62)***	1.87 (1.81-1.93)***	1.20 (1.18-1.22)***
Region 5	0.88 (0.86-0.91)***	1.35 (1.31-1.40)***	1.09 (1.07-1.11)***
Region 6	1.63 (1.58-1.68)***	1.95 (1.89-2.01)***	1.15 (1.13-1.17)***
Region 7	1.11 (1.06-1.16)***	2.15 (2.06-2.24)***	1.26 (1.23-1.29)***
Region 8	0.91 (0.87-0.97)**	3.35 (3.22-3.49)***	1.13 (1.10-1.16)***
Region 9	0.80 (0.78-0.83)***	1.12 (1.08-1.16)***	0.93 (0.91-0.95)***
Region 10	1.02 (0.98-1.07)	3.08 (2.97-3.21)***	1.07 (1.04-1.09)***
Unknown	1.32 (1.26-1.39)***	1.58 (1.50-1.66)***	1.07 (1.04-1.10)***
Delivery in State with ≥20% Hispanic Population	1.03 (1.02-1.05)***	0.88 (0.86-0.89)***	0.87 (0.87-0.88)***
Delivery in State with ≥20% Black Population	1.55 (1.52-1.58)***	1.25 (1.23-1.27)***	1.19 (1.17-1.20)***
Delivery in State with ≥15% Population in Poverty	1.67 (1.63-1.70)***	1.27 (1.25-1.30)***	1.31 (1.30-1.33)***
Delivery in State with ≥35% Women with College Degree or More	0.66 (0.65-0.68)***	0.73 (0.71-0.75)***	0.83 (0.82-0.84)***
Insurance Plan Type			
PPO	(ref.)	(ref.)	(ref.)
Comprehensive	0.88 (0.81-0.95)**	1.03 (0.96-1.10)	0.92 (0.88-0.96)***
HMO/EPO	0.87 (0.85-0.89)***	0.99 (0.97-1.01)	1.02 (1.01-1.03)***
POS	1.07 (1.05-1.11)***	0.97 (0.94-0.99)*	1.00 (0.99-1.02)
CDHP	0.97 (0.95-1.00)	1.11 (1.08-1.14)***	1.01 (1.00-1.03)
HDHP	0.80 (0.77-0.83)***	0.96 (0.93-0.99)**	0.90 (0.89-0.92)***
Unknown	1.10 (1.06-1.14)***	0.78 (0.75-0.81)***	1.02 (0.99-1.04)
Year of Delivery			
2011	1.17 (1.15-1.19)***	0.79 (0.77-0.80)***	1.02 (1.01-1.03)***
2012	1.09 (1.07-1.11)***	0.88 (0.86-0.89)***	1.03 (1.02-1.04)
2013	1.05 (1.03-1.07)***	0.99 (0.97-1.01)	1.12 (1.11-1.13)***
2014	0.97 (0.95-0.99)*	1.08 (1.06-1.10)***	1.04 (1.03-1.05)***
2015	0.89 (0.87-0.91)***	1.17 (1.14-1.19)***	0.97 (0.96-0.99)***
2016	0.83 (0.81-0.86)***	1.16 (1.14-1.19)***	0.94 (0.92-0.95)***
2017	0.78 (0.76-0.80)***	1.21 (1.18-1.24)***	0.75 (0.74-0.76)***
Delivery Mode			
Vaginal	(ref.)	(ref.)	(ref.)
Cesarean	7.82 (7.69-7.96)***	0.93 (0.92-0.95)***	1.07 (1.06-1.08)***
Non-Opioid Substance Use Disorder	0.98 (0.92-1.04)	1.36 (1.29-1.43)***	0.92 (0.89-0.96)***
Psychiatric Disorder, Any	1.19 (1.16-1.23)***	1.31 (1.28-1.35)***	1.00 (0.98-1.02)
Chronic Hypertension	1.87 (1.83-1.92)***	1.19 (1.17-1.22)***	1.07 (1.06-1.09)***

	Sterilization	LARC	Moderately Effective Methods
Gestational Hypertension	1.24 (1.21-1.27)***	1.19 (1.16-1.21)***	1.12 (1.11-1.14)***
Diabetes Mellitus	2.01 (1.95-2.06)***	0.86 (0.82-0.89)***	0.86 (0.84-0.88)***
Gestational Diabetes	1.63 (1.60-1.66)***	0.86 (0.84-0.87)***	0.91 (0.90-0.92)***
Asthma	1.09 (1.06-1.13)***	1.23 (1.19-1.27)***	1.09 (1.06-1.11)***
Autoimmune Disease	1.19 (1.13-1.24)***	0.95 (0.90-1.00)	0.92 (0.89-0.95)***
Hepatitis C	1.12 (0.87-1.44)	1.10 (0.87-1.39)	0.78 (0.66-0.92)**
Pain Condition	1.22 (1.19-1.26)***	1.26 (1.23-1.29)***	0.96 (0.95-0.98)***
Any ANC	1.19 (1.14-1.24)***	1.32 (1.27-1.38)***	1.18 (1.15-1.20)***
Postpartum Care Visit within 60 Days of Delivery	1.29 (1.27-1.31)***	11.13 (10.90-11.36)***	1.41 (1.40-1.42)***

**p<0.05, **p<0.01, ***p<<0.001*

In the fully adjusted multinomial model (Table 4.8), women with each type of opioid use during pregnancy had significantly higher relative risks of receiving sterilization relative to no prescription method compared with women who did not use opioids during pregnancy. This finding was also noted in the unadjusted analysis. Women with chronic prescription opioid use during pregnancy had the highest aRRR for sterilization relative to no prescription method (aRRR: 2.12, 95% CI: 1.99-2.26). In the fully adjusted analysis, the relative risk for provision of LARC or MEM relative to no method did not differ significantly for women with chronic prescription opioid use compared with women who did not use opioids during pregnancy. As observed in the unadjusted analysis, the risk of provision of sterilization, LARC, and MEM relative to no method was significantly higher for women with non-chronic prescription opioid use than for women who did not use opioids during pregnancy. Women with OUD/Bup had significantly higher relative risks for provision of sterilization, and significantly lower relative risks for provision of LARC and MEM relative to the provision of no prescription method compared with women who did not use opioids during pregnancy. This finding represents a shift from the unadjusted analysis in which women with OUD/Bup had a non-significantly higher RRR for LARC provision compared with no method. In the fully adjusted model, women with an OUD diagnosis/buprenorphine prescription had an aRRR of 0.73 (95% CI: 0.65-0.82) for

receipt of LARC verses no method and an aRRR of 0.73 (95% CI: 0.68-0.79) for receipt of MEM verses no method.

The patterns for aRRRs among the different age groups were the same for the unadjusted and adjusted models. The aRRR for sterilization verses no method increased with age; the aRRR for LARC verses no method decreased with age; and the aRRR for MEM verses no method was lower for each age group in comparison to the reference group (25-29 years). Across HRSA regions, associations remained largely the same between the adjusted and unadjusted models. The aRRR for sterilization ranged from a low of 0.54 in Region 2 (NY, NJ, PR) (95% CI: 0.52-0.56) to a high of 1.35 in Region 6 (LA, AR, OK, TX, NM) (95% CI: 1.28-1.43). All regions except Region 2 (NY, NJ, PR) and 5 (MN, WI, IL, IN, MI, OH) had a significantly increased aRRR for LARC relative to no provision compared with the reference region, Region 3. The aRRR for MEM provision was significantly increased for all regions relative to Region 3 (PA, MD, DE, VA, WV) except Regions 1 (ME, NH, VT, MA, RI, CT) and 2 (NY, NJ, PR).

The RRRs varied significantly by the state-level characteristics. The adjusted RRRs and unadjusted RRRs for women who delivered in states with 20% or more Hispanic population were similar in magnitude and effect, higher RRRs for sterilization and lower RRRs for LARC and MEM. The fully adjusted results for women who delivered in states with 20% or more Black population changed substantively from the unadjusted analysis. They had a significantly higher aRRR for sterilization and a significantly lower aRRR for LARC verses no methods, but no significant difference for MEM provision verses no method in the fully adjusted model. Women living in states with 15% or more of the population living in poverty had significantly higher aRRRs for sterilization and MEM provision verses no method and significantly lower aRRR for LARC provision verses no method. Compared with the unadjusted models, the aRRRs

for women in states where 35% or more of women have at least a college degree were similar but attenuated, with significantly lower aRRRs for sterilization and LARC verses no method, and no significant differences for MEM provision. Finally, trends across the study time period were the same in the adjusted and unadjusted models. The aRRR for sterilization decreased over the study period while the aRRR for LARC provision increased; the aRRR for MEM provision was significantly higher relative to 2011 from 2012-14, but it was significantly lower beginning in 2015.

Several chronic disease and clinical variables were significant in the fully adjusted model. Women with non-opioid SUDs, psychiatric disorders, chronic hypertension, diabetes mellitus, gestational diabetes, asthma, and pain conditions had significantly higher aRRRs for sterilization verses no prescription method. Women with gestational hypertension and autoimmune disease had significantly lower aRRRs for sterilization. Women with psychiatric disorders, chronic hypertension, and asthma had significantly higher aRRRs for LARC verses no method, while those with gestational diabetes had a significantly lower aRRR. Women with chronic hypertension, gestation hypertension, and asthma had significantly higher aRRRs for MEM provision verses no method; women with non-opioid SUD, diabetes mellitus, gestational diabetes, and with a pain condition had significantly lower aRRRs for MEM provision verses no method. The remaining conditions were not significantly related to method type. Finally, women who had a postpartum care visit within 60 days of delivery had significantly higher aRRRs for sterilization, LARC, and MEM, with a pronounced relationship for LARC provision (aRRR: 10.98, 95% CI: 10.75-11.20).

Table 4.8 Multinomial Results: Adjusted Relative Risk Ratios for Provision of Contraception within 60 Days Postpartum, Relative to No Provision, by Method Type (N=1,291,352)

	Sterilization	LARC	Moderately Effective Methods
Opioid Use			
No Opioid Use During Pregnancy	(ref.)	(ref.)	(ref.)
Non-Chronic Prescription Opioid Use	1.49 (1.46-1.53)***	1.10 (1.07-1.12)***	1.05 (1.03-1.06)***
Chronic Prescription Opioid Use	2.12 (1.99-2.26)***	0.97 (0.89-1.06)	0.98 (0.93-1.03)
OUD Diagnosis/Buprenorphine Prescription	1.32 (1.16-1.50)***	0.73 (0.65-0.82)***	0.73 (0.68-0.79)***
Age, Categorical			
<20	0.01 (0.01-0.02)***	1.68 (1.62-1.74)***	0.89 (0.87-0.91)***
20-24	0.48 (0.46-0.50)***	1.39 (1.36-1.42)***	0.94 (0.93-0.96)***
25-29	(ref.)	(ref.)	(ref.)
30-34	1.51 (1.48-1.55)***	0.73 (0.71-0.74)***	0.82 (0.81-0.83)***
35-39	2.42 (2.37-2.48)***	0.52 (0.51-0.53)***	0.58 (0.57-0.59)***
40+	2.72 (2.63-2.80)***	0.32 (0.30-0.33)***	0.36 (0.35-0.37)***
HRSA Region			
Region 1	0.69 (0.66-0.73)***	1.46 (1.39-1.54)***	0.97 (0.95-1.00)
Region 2	0.54 (0.52-0.56)***	0.52 (0.49-0.55)***	0.77 (0.76-0.79)***
Region 3	(ref.)	(ref.)	(ref.)
Region 4	1.21 (1.15-1.27)***	1.59 (1.51-1.67)***	1.16 (1.13-1.19)***
Region 5	0.91 (0.87-0.94)***	1.01 (0.97-1.04)	1.06 (1.04-1.08)***
Region 6	1.35 (1.28-1.43)***	2.08 (1.96-2.20)***	1.24 (1.20-1.28)***
Region 7	1.26 (1.20-1.33)***	1.61 (1.54-1.69)***	1.23 (1.19-1.26)***
Region 8	1.16 (1.09-1.23)***	3.04 (2.91-3.18)***	1.20 (1.16-1.23)***
Region 9	0.67 (0.63-0.71)***	1.34 (1.26-1.43)***	1.12 (1.09-1.16)***
Region 10	1.14 (1.08-1.20)***	2.34 (2.24-2.44)***	1.06 (1.03-1.09)***
Unknown	1.25 (1.18-1.31)***	1.49 (1.41-1.57)***	1.07 (1.03-1.10)***
Delivery in State with ≥20% Hispanic Population	1.10 (1.06-1.15)***	0.72 (0.69-0.75)***	0.84 (0.82-0.86)***
Delivery in State with ≥20% Black Population	1.14 (1.10-1.17)***	0.88 (0.86-0.91)***	0.99 (0.97-1.01)
Delivery in State with ≥15% Population in Poverty	1.35 (1.31-1.39)***	0.91 (0.88-0.94)***	1.12 (1.10-1.14)***
Delivery in State with ≥35% Women with College Degree or More	0.79 (0.76-0.83)***	0.91 (0.88-0.95)***	1.02 (0.99-1.04)
Insurance Plan Type			
PPO	(ref.)	(ref.)	(ref.)
Comprehensive	1.20 (1.11-1.30)***	0.82 (0.76-0.88)***	0.91 (0.87-0.94)***
HMO/EPO	0.93 (0.90-0.95)***	1.07 (1.05-1.10)***	1.07 (1.05-1.08)***
POS/POS + Capitation	0.99 (0.96-1.02)	0.98 (0.95-1.01)	1.01 (0.99-1.02)
CDHP	0.99 (0.96-1.02)	1.01 (0.99-1.04)	1.02 (1.00-1.03)*
HDHP	0.92 (0.89-0.95)***	0.93 (0.90-0.96)***	0.96 (0.94-0.98)***
Unknown	1.16 (1.11-1.22)***	0.96 (0.91-1.01)	1.06 (1.04-1.09)***
Year of Delivery			
2011	Omitted	Omitted	Omitted

	Sterilization	LARC	Moderately Effective Methods
2012	0.96 (0.94-0.99)**	1.10 (1.07-1.12)***	1.01 (0.99-1.02)
2013	0.96 (0.94-0.99)**	1.19 (1.16-1.22)***	1.10 (1.08-1.11)***
2014	0.88 (0.86-0.91)***	1.31 (1.28-1.34)***	1.03 (1.02-1.05)***
2015	0.79 (0.76-0.81)***	1.34 (1.30-1.37)***	0.95 (0.94-0.97)***
2016	0.73 (0.71-0.75)***	1.32 (1.29-1.36)***	0.92 (0.91-0.94)***
2017	0.68 (0.66-0.70)***	1.37 (1.33-1.41)***	0.75 (0.73-0.76)***
Delivery Mode			
Vaginal	(ref.)	(ref.)	(ref.)
Cesarean	6.75 (6.63-6.87)***	0.99 (0.98-1.01)	1.11 (1.10-1.120)***
Non-Opioid Substance Use Disorder	1.19 (1.11-1.29)***	1.00 (0.94-1.06)	0.92 (0.88-0.96)***
Psychiatric Disorder, Any	1.08 (1.05-1.12)***	1.14 (1.11-1.17)***	1.02 (1.00-1.04)
Chronic Hypertension	1.29 (1.25-1.32)***	1.11 (1.08-1.14)***	1.04 (1.02-1.06)***
Gestational Hypertension	0.75 (0.73-0.77)***	1.00 (0.97-1.02)	1.06 (1.05-1.09)***
Diabetes Mellitus	1.19 (1.15-1.23)***	0.96 (0.93-1.01)	0.92 (0.88-0.96)***
Gestational Diabetes	1.13 (1.11-1.16)***	0.92 (0.90-0.94)***	0.94 (0.93-0.95)***
Asthma	1.06 (1.02-1.10)**	1.11 (1.07-1.14)***	1.09 (1.07-1.11)***
Autoimmune Disease	0.93 (0.89-0.98)*	0.98 (0.93-1.03)	0.97 (0.94-1.00)
Pain Condition	1.11 (1.08-1.14)***	1.02 (1.00-1.05)	0.96 (0.94-0.97)***
Postpartum Care Visit within 60 Days of Delivery	1.21 (1.19-1.22)***	10.98 (10.75-11.21)***	1.40 (1.39-1.41)***

**p<0.05, **p<0.01, ***p<<0.001*

Model Fit Diagnostics

The model fit diagnostics used to evaluate the multinomial models involved a combination of AIC and BIC to assess model fit and the same method of model building was applied, as used for the multivariable logistic regressions. The final model had an AIC of 1.819 and a BIC of -1.582e+07, the lowest AIC and BIC of the four models included in Table 4.9.

Table 4.9 Aim 1 Multinomial Logistic Regression Model Fit Diagnostics

	Model Description	BIC	AIC
Model 1	Demographic variables (Maternal Age, HRSA Region, State Characteristics, Insurance Place Type, Year of Delivery)	-1.568e+07	1.928
Model 2	Model 1 + Opioid Use	-1.568e+07	1.926
Model 3	Model 2 + Chronic Conditions	-1.569e+07	1.923
Model 4 (Final)	Model 3 + Delivery Mode + PNC visit	-1.582e+07	1.819

Aim 1 Sensitivity Analysis

A sensitivity analysis was done comparing women who met the inclusion criteria for Aim 1 and those who did not to ensure there were no major differences between these groups. Table 4.10 displays the descriptive characteristics for women who met the Aim 1 inclusion criteria, of women who did not meet the inclusion criteria, and all women with a livebirth captured in the MarketScan database between January 01, 2011 and December 31st, 2017.

Women were included in the Aim 1 analysis if they had a livebirth between January 1st, 2011 and November 1st, 2017, and maintained continuous health and pharmaceutical insurance coverage for the duration of pregnancy and for at least the first 60 days postpartum. Of the approximately 2.3 million live births identified in the MarketScan database, nearly 55% met the inclusion criteria for Aim 1. Overall, there were no significant differences in the characteristics of women who did and did not meet the inclusion criteria, however, only variables captured at the time of delivery were examined.

Table 4.10 Sensitivity Analysis: Characteristics of Women with a Livebirth During Study Period (January 2011-November 2017), by Inclusion Criteria*

	Met Aim 1 Inclusion Criteria	Did Not Meet Aim 1 Inclusion Criteria	Full Sample with Live Birth
Total N's (%)	1,291,352 (54.5%)	1,075,511 (45.5%)	2,366,863 (100%)
Age, mean years (SD)	30.3 (5.5)	29.7 (5.5)	30.0 (5.5)
Age, Categorical			
<20	2.9% (36,882)	2.9% (31,623)	2.9% (68,505)
20-24	12.3% (159,196)	14.8% (158,752)	13.4% (317,948)
25-29	27.6% (356,299)	30.4% (326,761)	28.9% (683,060)
30-34	35.3% (455,415)	32.9% (353,594)	34.2% (809,009)
35-39	17.6% (227,946)	15.4% (165,647)	16.6% (393,593)
40+	4.3% (55,614)	3.6% (39,134)	4.0% (94,748)
HRSA Region			
Region 1	4.3% (55,782)	3.7% (39,467)	4.0% (95,249)
Region 2	7.5% (97,282)	9.1% (97,508)	8.2% (194,790)
Region 3	8.6% (111,514)	9.4% (101,480)	9.0% (212,994)
Region 4	21.7% (280,470)	18.7% (200,802)	20.3% (481,272)
Region 5	18.3% (236,920)	18.3% (197,085)	18.3% (434,005)
Region 6	13.2% (170,845)	13.6% (146,630)	13.4% (317,475)
Region 7	4.1% (52,726)	3.8% (40,579)	3.9% (93,305)

	Met Aim 1 Inclusion Criteria	Did Not Meet Aim 1 Inclusion Criteria	Full Sample with Live Birth
Region 8	3.2% (41,104)	3.0% (32,097)	3.1% (73,201)
Region 9	12.0% (155,183)	11.3% (121,373)	11.7% (276,556)
Region 10	4.0% (51,831)	3.3% (35,115)	3.7% (86,946)
Unknown	2.9% (37,695)	5.9% (63,375)	4.3% (101,070)
Delivery in State with ≥20% Hispanic Population	29.4% (380,268)	27.7% (297,533)	28.6% (677,801)
Delivery in State with ≥20% Black Population	16.6% (214,766)	14.7% (158,333)	15.8% (373,099)
Delivery in State with ≥15% Population in Poverty	13.5% (174,548)	13.9% (149,827)	13.7% (324,375)
Delivery in State with ≥35% Women with College Degree or More	10.1% (130,623)	8.9% (95,872)	9.6% (226,495)
Insurance Plan Type			
PPO	59.4% (767,515)	62.1% (668,063)	60.7% (1,435,578)
Comprehensive	1.0% (13,122)	0.7% (7,932)	0.9% (21,054)
HMO/EPO	14.7% (189,842)	14.2% (152,639)	14.5% (342,481)
POS/POS+Capitation	7.3% (94,444)	6.0% (64,606)	6.7% (159,050)
CDHP	8.2% (105,445)	4.9% (52,470)	6.7% (157,915)
HDHP	6.1% (78,302)	5.5% (58,985)	5.8% (137,287)
Unknown	3.3% (42,682)	6.6% (70,816)	4.8% (113,498)
Year of Delivery			
2011	20.9% (270,505)	20.6% (221,639)	20.8% (492,144)
2012	20.1% (260,183)	20.4% (218,964)	20.2% (479,147)
2013	15.0% (194,041)	16.7% (179,435)	15.8% (373,476)
2014	14.1% (182,215)	18.0% (193,733)	15.9% (375,948)
2015	11.2% (144,467)	7.4% (79,571)	9.5% (224,038)
2016	10.6% (136,978)	7.5% (80,613)	9.2% (217,591)
2017	8.0% (102,963)	9.4% (101,556)	8.6% (204,519)
Delivery Mode			
Vaginal	64.5% (832,323)	65.3% (702,673)	64.8% (1,534,996)
Cesarean	35.5% (459,029)	34.7% (372,838)	35.1% (831,867)

**Notes for Table 4.10: only variables measured at time of delivery are assessed because this table includes women who did not meet inclusion criteria and therefore, did not have prenatal/postpartum data consistently available.*

4.4 Aim 2 Results

As with Aim 1, the primary independent variable in the Aim 2 cohort was opioid use during pregnancy. The prevalence of opioid use during pregnancy was similar to the levels observed in the Aim 1 cohort, with 89.9% of women having no evidence of opioid use during pregnancy, approximately 9% with evidence of non-chronic prescription opioid use, 0.8% with chronic prescription opioid use, and 0.4% with OUD/Bup (Table 4.11). The prevalence and

distribution of opioid use across the covariates in Aim 2 were consistent with the patterns observed in the Aim 1 cohort.

Table 4.11 Characteristics of Aim 2 Cohort by Type of Opioid Use During Pregnancy, Row Totals

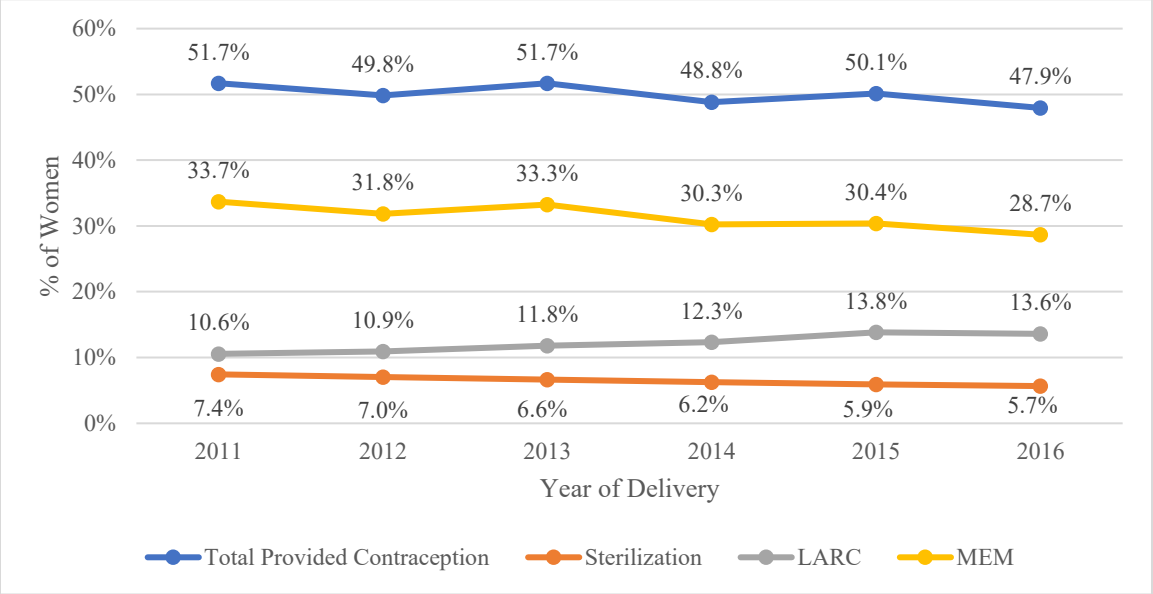
	No Opioid Use During Pregnancy	Non-chronic Prescription Opioid Use	Chronic Prescription Opioid Use	OUD Diagnosis or Buprenorphine Prescription
Total N (%)	1,142,594 (89.9%)	113,273 (8.9%)	9,838 (0.8%)	5,127 (0.4%)
Age, mean years (SD)	30.3 (5.4)	30.0 (5.7)	31.4 (5.6)	26.5 (5.9)
Age, Categorical				
<20	88.4% (32,798)	10.1% (3,735)	0.3% (123)	1.2% (433)
20-24	87.4% (138,270)	10.7% (16,891)	0.6% (1,007)	1.2% (1,963)
25-29	90.1% (319,420)	8.9% (31,408)	0.7% (2,514)	0.3% (1,141)
30-34	90.8% (404,560)	8.2% (36,639)	0.8% (3,398)	0.2% (987)
35-39	90.0% (199,399)	8.8% (19,524)	0.9% (2,108)	0.2% (495)
40+	89.1% (48,147)	9.4% (5,076)	1.3% (688)	0.2% (108)
HRSA Region				
Region 1	92.5% (51,123)	6.5% (3,613)	0.5% (256)	0.5% (262)
Region 2	94.2% (88,321)	4.9% (4,588)	0.4% (420)	0.5% (454)
Region 3	91.1% (101,337)	7.6% (8,491)	0.7% (830)	0.6% (624)
Region 4	87.9% (233,441)	10.8% (28,693)	0.8% (2,245)	0.4% (1,081)
Region 5	90.7% (214,663)	8.1% (19,211)	0.8% (1,797)	0.5% (1,060)
Region 6	88.1% (149,436)	10.7% (18,186)	0.9% (1,518)	0.3% (503)
Region 7	89.4% (45,819)	9.5% (4,877)	0.8% (406)	0.2% (130)
Region 8	89.7% (36,740)	9.2% (3,758)	0.8% (330)	0.3% (141)
Region 9	90.1% (139,540)	8.8% (13,680)	0.8% (1,267)	0.3% (419)
Region 10	90.2% (45,271)	8.4% (4,244)	0.8% (398)	0.6% (297)
Unknown	89.2% (36,863)	9.5% (3,932)	0.9% (371)	0.4% (156)
Delivery in State with ≥20% Hispanic Population				
Yes	89.5% (335,333)	9.4% (35,337)	0.8% (2,949)	0.3% (1,051)
No	90.1% (807,261)	8.7% (77,936)	0.8% (6,889)	0.5% (4,076)
Delivery in State with ≥20% Black Population				
Yes	88.0% (177,889)	10.8% (21,852)	0.9% (1,747)	0.4% (733)
No	90.3% (964,705)	8.6% (91,421)	0.8% (8,091)	0.4% (4,394)
Delivery in State with ≥15% Population in Poverty				
Yes	87.9% (146,792)	10.6% (17,722)	1.0% (1,603)	0.5% (896)
No	90.2% (995,802)	8.7% (95,551)	0.7% (8,235)	0.4% (4,231)
Delivery in State with ≥35% Women with College Degree or More				
Yes	91.7% (117,184)	7.3% (9,357)	0.6% (723)	0.4% (495)
No	89.7% (1,025,410)	9.1% (103,916)	0.8% (9,115)	0.4% (4,632)
Insurance Plan Type				
PPO	89.8% (686,956)	8.9% (68,490)	0.8% (6,250)	0.4% (3,117)
Comprehensive	87.9% (10,130)	9.6% (1,107)	1.3% (151)	1.2% (135)
HMP/EPO	89.4% (169,779)	9.5% (18,003)	0.7% (1,375)	0.4% (658)
POS	89.5% (82,454)	9.3% (8,579)	0.7% (674)	0.4% (403)
CDHP	90.4% (86,189)	8.6% (8,190)	0.7% (635)	0.4% (367)
HDHP	91.8% (65,523)	7.3% (5,249)	0.6% (398)	0.3% (215)
Unknown	90.7% (41,563)	8.0% (3,655)	0.8% (355)	0.5% (232)
Year of Delivery				
2011	88.8% (251,027)	10.1% (28,517)	0.8% (2,329)	0.3% (797)
2012	89.2% (253,071)	9.5% (27,088)	0.8% (2,359)	0.4% (1,034)

	No Opioid Use During Pregnancy	Non-chronic Prescription Opioid Use	Chronic Prescription Opioid Use	OUD Diagnosis or Buprenorphine Prescription
2013	89.6% (184,301)	9.2% (18,839)	0.8% (1,646)	0.4% (893)
2014	90.3% (181,569)	8.4% (16,912)	0.8% (1,599)	0.5% (977)
2015	91.1% (138,442)	7.7% (11,698)	0.7% (1,055)	0.5% (743)
2016	91.9% (134,184)	7.0% (10,219)	0.6% (850)	0.5% (683)
Delivery Mode				
Vaginal	91.2% (746,720)	7.8% (63,909)	0.6% (5,278)	0.4% (3,238)
Cesarean	87.6% (395,874)	10.9% (49,364)	1.0% (4,560)	0.4% (1,889)
Non-Opioid SUD				
Yes	62.9% (10,720)	11.7% (1,992)	4.0% (686)	21.4% (3,646)
No	90.3% (1,131,874)	8.9% (111,281)	0.7% (9,152)	0.1% (1,481)
Psychiatric Disorder, Any				
Yes	80.7% (56,730)	14.2% (10,013)	2.7% (1,921)	2.3% (1,645)
No	90.4% (1,085,864)	8.6% (103,260)	0.7% (7,917)	0.3% (3,482)
Chronic Hypertension				
Yes	85.4% (90,270)	12.4% (13,144)	1.6% (1,733)	0.5% (515)
No	90.3% (1,052,324)	8.6% (100,129)	0.7% (8,105)	0.4% (4,612)
Gestational Hypertension				
Yes	86.6% (133,295)	11.7% (17,970)	1.2% (1,922)	0.4% (667)
No	90.4% (1,009,299)	8.5% (95,303)	0.7% (7,916)	0.4% (4,460)
Diabetes Mellitus				
Yes	86.7% (46,699)	11.5% (6,192)	1.4% (738)	0.4% (214)
No	90.0% (1,095,895)	8.8% (107,081)	0.7% (9,100)	0.4% (4,913)
Gestational Diabetes				
Yes	88.7% (165,913)	10.1% (18,879)	1.0% (1,796)	0.3% (543)
No	90.1% (976,681)	8.7% (94,394)	0.7% (8,042)	0.4% (4,584)
Asthma				
Yes	84.7% (51,468)	13.2% (8,008)	1.5% (903)	0.7% (412)
No	90.2% (1,091,126)	8.7% (105,265)	0.7% (8,935)	0.4% (4,715)
Autoimmune Disease				
Yes	83.6% (20,014)	12.3% (2,955)	3.2% (769)	0.8% (187)
No	90.0% (1,122,580)	8.8% (110,318)	0.7% (9,069)	0.4% (4,940)
Pain Condition				
Yes	78.2% (76,196)	17.4% (16,965)	3.4% (3,343)	1.0% (974)
No	90.9% (1,066,398)	8.2% (96,308)	0.5% (6,495)	0.4% (4,153)
Hepatitis C				
Yes	59.2% (515)	9.8% (85)	1.3% (11)	29.8% (259)
No	89.9% (1,142,079)	8.9% (113,188)	0.8% (9,827)	0.4% (4,868)
Any ANC				
Yes	89.8% (1,102,704)	9.0% (110,236)	0.8% (9,558)	0.4% (4,967)
No	92.0% (39,890)	7.0% (3,037)	0.6% (280)	0.4% (160)
Contraceptive provision within 365 Days Postpartum				
No Evidence of Provision	91.2% (576,902)	7.8% (49,354)	0.6% (4,125)	0.4% (2,433)
Evidence of Provision	88.7% (565,692)	10.0% (63,919)	0.9% (5,713)	0.4% (2,694)
Sterilization	83.8% (70,762)	13.8% (11,679)	1.9% (1,612)	0.5% (397)
LARC	88.6% (133,652)	10.1% (15,196)	0.8% (1,178)	0.5% (750)
Moderately Effective Methods	89.7% (361,278)	9.2% (37,044)	0.7% (2,923)	0.4% (1,547)

Dependent Variable: Postpartum prescription Contraceptive Provision

The Aim 2 dependent variable was time to contraceptive provision within the first 365 days postpartum. In the Aim 2 cohort, 50.2% of women were provided prescription contraception within 365 days postpartum (Table 4.12), with the majority receiving a MEM. Trends in provision over the study period were similar to those observed in Aim 1 with sterilization declining (p for tend<0.00), LARC provision increasing (p for tend<0.00), and variable MEM provision with a decline in the final study year (Figure 4.5). For all measured variables, levels of contraceptive provision increased compared with levels observed in Aim 1 because of the extended postpartum observation period in Aim 2.

Figure 4.5 Trends for Provision of Prescription Contraception within 365 Days Postpartum, overall and by Method Type, Aim 2 Cohort



Levels of contraceptive provision by the different categories of opioid use were similar to those in Aim 1 with some noticeable exceptions. Overall, women with chronic prescription opioid use had the highest levels of contraceptive provision and women with no opioid use during pregnancy, the lowest levels of provision- a change from Aim 1 in which the OUD/Bup

group had the lowest level of contraceptive provision. Women across all categories of opioid use continued to have higher levels of sterilization than women who did not use opioids, with the highest prevalence among women with chronic prescription opioid use. LARC provision was also higher across all categories of opioid use compared with no opioid use during pregnancy. Unlike for Aim 1 where women with non-chronic prescription opioid use had the highest levels of LARC provision, women in the OUD/Bup group had the highest prevalence of LARC provision among the Aim 2 cohort. Finally, MEM provision was relatively consistent across groups, at approximately 30%.

Patterns for age and by geographic region across the different contraceptive method types were similar to those noted in Aim 1. Older women had the highest prevalence of sterilization while younger women, higher levels of LARC provision. Levels of sterilization and LARC varied by geographic regions while MEM provision was more consistent. For most comorbidities, women with the morbidity had higher levels of contraceptive provision than women without the morbidity but the relationships were not as consistent as in Aim 1. Women with non-opioid SUD, diabetes, gestational diabetes, autoimmune disorders, and hepatitis C had lower levels of contraceptive provision than women who did not have these conditions. Conversely, women with psychiatric diagnoses, chronic and gestational hypertension, asthma, and pain conditions had higher contraceptive provision than women who did not have these conditions. Women with cesarean deliveries had substantially higher levels of contraceptive provision than women with vaginal deliveries, largely due to high levels of sterilization.

Table 4.12 Characteristics of Aim 2 Cohort by Postpartum Contraceptive Method Within 365 Days Postpartum, Row Totals

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	Moderately Effective Methods
Total N (%)	632,814 (49.8%)	638,018 (50.2%)	84,450 (6.6%)	150,776 (11.9%)	402,792 (31.7%)
Opioid Use					
No Opioid Use During Pregnancy	50.5% (576,902)	49.5% (565,692)	6.2% (70,762)	11.7% (133,652)	31.6% (361,278)
Non-Chronic Prescription Opioid Use	43.6% (49,354)	56.4% (63,919)	10.3% (11,679)	13.4% (15,196)	32.7% (37,044)
Chronic Prescription Opioid Use	41.9% (4,125)	58.1% (5,713)	16.4% (1,612)	12.0% (1,178)	29.7% (2,923)
OUD Diagnosis/ Buprenorphine Prescription	47.4% (2,433)	52.5% (2,694)	7.7% (397)	14.6% (750)	30.2% (1,547)
Age, mean years (SD)	30.8 (5.5)	29.7 (5.4)	33.4 (4.5)	28.6 (5.5)	29.3 (5.2)
Age, Categorical					
<20	39.1% (14,521)	60.8% (22,568)	0.05% (17)	22.2% (8,238)	38.6% (14,313)
20-24	42.7% (67,599)	57.2% (90,532)	2.0% (3,196)	18.3% (28,903)	36.9% (58,433)
25-29	46.9% (166,141)	53.1% (188,342)	4.2% (14,926)	12.8% (45,541)	36.1% (127,875)
30-34	51.2% (227,945)	48.8% (217,639)	6.9% (30,666)	10.5% (46,700)	31.5% (140,273)
35-39	55.6% (123,195)	44.4% (98,331)	12.2% (27,004)	8.3% (18,298)	23.9% (53,029)
40+	61.8% (33,413)	38.1% (20,606)	16.0% (8,641)	5.7% (3,096)	16.4% (8,869)
HRSA Region					
Region 1	52.3% (28,916)	47.7% (26,338)	4.1% (2,291)	13.5% (7,440)	30.1% (16,607)
Region 2	60.9% (56,922)	39.1% (36,463)	4.4% (4,069)	7.7% (7,168)	27.0% (25,226)
Region 3	52.7% (58,621)	47.3% (52,701)	6.4% (7,102)	9.1% (10,182)	31.8% (35,417)
Region 4	44.2% (117,332)	55.8% (148,128)	8.7% (23,211)	13.1% (34,672)	34.0% (90,245)
Region 5	51.3% (121,377)	48.7% (115,354)	5.5% (12,930)	10.5% (24,984)	32.7% (77,440)
Region 6	46.0% (78,077)	54.0% (91,566)	9.1% (15,414)	12.7% (21,482)	32.2% (54,670)
Region 7	45.4% (23,257)	54.6% (27,975)	6.4% (3,268)	13.7% (7,020)	34.5% (17,687)
Region 8	46.2% (18,910)	53.8% (22,059)	5.0% (2,032)	19.2% (7,865)	29.7% (12,162)
Region 9	54.4% (84,335)	45.6% (70,571)	5.3% (8,178)	10.4% (16,061)	29.9% (46,332)
Region 10	46.6% (23,415)	53.4% (26,795)	5.6% (2,812)	18.7% (9,375)	29.1% (14,608)
Unknown	51.9% (21,652)	48.1% (20,068)	7.5% (3,143)	10.8% (4,527)	29.7% (12,398)
Delivery in State with ≥20% Hispanic Population					
Yes	51.4% (192,501)	48.6% (182,169)	6.5% (58,099)	11.9% (107,049)	32.4% (290,701)
No	49.1% (440,313)	50.9% (455,849)	7.0% (26,351)	11.7% (43,727)	29.9% (112,091)
Delivery in State with ≥20% Black Population					
Yes	44.1% (89,115)	55.9% (113,106)	8.7% (17,703)	12.6% (25,393)	34.6% (70,010)
No	50.9% (543,699)	49.1% (524,912)	6.2% (66,747)	11.7% (125,383)	31.1% (332,782)
Delivery in State with ≥15% Population in Poverty					
Yes	42.7% (71,373)	57.3% (95,640)	6.3% (69,224)	11.8% (130,371)	31.0% (342,782)
No	50.9% (561,441)	49.1% (542,378)	9.1% (15,226)	12.2% (20,405)	35.9% (60,009)
Delivery in State with ≥35% Women with College Degree or More					
Yes	53.7% (68,620)	46.3% (59,139)	6.8% (78,095)	11.9% (136,064)	31.9% (364,720)
No	49.4% (564,194)	50.6% (578,879)	5.0% (6,355)	11.5% (14,712)	29.8% (38,072)
Year of Delivery					
2011	48.3% (136,538)	51.7% (146,132)	7.4% (21,036)	10.6% (29,847)	33.7% (95,249)
2012	50.2% (142,269)	49.8% (141,283)	7.0% (19,941)	10.9% (31,032)	31.8% (90,310)
2013	48.3% (99,366)	51.7% (106,313)	6.6% (13,641)	11.8% (24,231)	33.3% (68,441)

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	Moderately Effective Methods
2014	51.2% (102,902)	48.8% (98,155)	6.2% (12,555)	12.3% (24,778)	30.2% (60,822)
2015	49.9% (75,764)	50.1% (76,174)	5.9% (9,016)	13.8% (21,012)	30.4% (46,146)
2016	52.1% (75,975)	47.9% (69,961)	5.7% (8,261)	13.6% (19,876)	28.7% (41,824)
Delivery Mode					
Vaginal	52.0% (426,070)	48.0% (393,070)	2.6% (21,153)	12.8% (105,183)	32.6% (266,739)
Cesarean	45.8% (206,744)	54.2% (244,943)	14.0% (63,297)	10.1% (45,593)	30.1% (136,053)
Non-Opioid SUD					
Yes	49.8% (625,045)	50.2% (628,743)	6.6% (83,298)	11.8% (148,079)	31.7% (397,266)
No	45.6% (7,769)	54.4% (9,275)	6.8% (1,152)	15.8% (2,697)	31.8% (5,426)
Psychiatric Disorder, Any					
Yes	46.5% (32,679)	53.5% (37,630)	7.7% (5,441)	14.7% (10,305)	31.1% (21,884)
No	50.0% (600,135)	50.0% (600,388)	6.6% (79,009)	11.7% (140,471)	31.7% (380,908)
Chronic Hypertension					
Yes	45.7% (48,304)	54.3% (57,358)	10.7% (11,353)	12.3% (13,043)	31.2% (32,962)
No	50.2% (584,510)	49.8% (580,660)	6.3% (73,097)	11.8% (137,733)	31.7% (369,830)
Gestational Hypertension					
Yes	46.7% (71,797)	53.3% (82,057)	7.6% (11,736)	12.5% (19,268)	33.2% (51,053)
No	50.2% (561,017)	49.8% (555,961)	6.5% (72,714)	11.8% (131,508)	31.5% (351,739)
Diabetes Mellitus					
Yes	50.1% (26,979)	49.9% (26,864)	12.4% (6,670)	10.2% (5,507)	27.3% (14,687)
No	49.8% (605,835)	50.2% (611,154)	6.4% (77,780)	11.9% (145,269)	31.9% (388,105)
Gestational Diabetes					
Yes	50.5% (94,503)	49.5% (92,628)	9.8% (18,328)	10.5% (19,571)	29.2% (54,729)
No	49.7% (538,311)	50.3% (545,390)	6.1% (66,122)	12.1% (131,205)	32.1% (348,063)
Asthma					
Yes	46.7% (28,411)	53.3% (32,380)	6.9% (4,211)	13.4% (8,119)	33.0% (20,050)
No	49.9% (604,403)	50.1% (605,638)	6.6% (80,239)	11.8% (142,657)	31.6% (382,742)
Autoimmune Disease					
Yes	50.3% (12,033)	49.7% (11,892)	7.9% (1,902)	11.7% (2,812)	30.0% (7,178)
No	49.8% (620,781)	50.2% (626,126)	6.6% (82,548)	11.9% (147,964)	31.7% (395,614)
Pain Condition					
Yes	47.8% (46,631)	52.2% (50,847)	8.1% (7,856)	13.8% (13,481)	30.3% (29,510)
No	50.0% (586,183)	50.0% (587,171)	6.5% (76,594)	11.7% (137,295)	31.8% (373,282)
Hepatitis C					
Yes	51.9% (452)	48.0% (418)	7.9% (69)	12.9% (112)	27.2% (237)
No	49.8% (632,362)	50.2% (637,600)	6.6% (84,381)	11.9% (150,664)	31.7% (402,555)

Aim 2: Univariate Analysis

The univariate analysis for Aim 2 began by calculating the mean time to contraceptive provision among women who ultimately received contraception during the study period (Table 4.13). This measure provided a crude estimate of time to first contraceptive provision conditioned on receiving contraception. A table with a limited set of covariates is presented below; a table with the full listing of covariates can be found in Appendix C. Average time to

provision varied by opioid use group with both the non-chronic and chronic prescription use group having average times to provision less than 60 days postpartum. Women in the OUD/Bup group, on average, did not receive contraception until 72.3 days postpartum (95% CI: 69.54-75.10). Time to first provision also varied substantially by method type with sterilization occurring, on average, 13.3 days after delivery (95% CI: 12.98-13.54), and LARC and MEM both having average times to provision exceeding 60 days. Time to provision decreased with age, with the oldest age group receiving contraception 25 days, on average, before the youngest age group, most likely due to their greater use of sterilization. Finally, for most comorbidities, except non-opioid SUDs, psychiatric disorders, and hepatitis C, the mean time to contraceptive provision was shorter for women with the comorbidity than for those without it.

Table 4.13 Unadjusted Mean Time to Contraceptive Provision in Women Provided Contraception Within 365 Days Postpartum

Covariates	Mean Days to Contraceptive Provision (95% CI)
Opioid Use During Pregnancy	
No use	61.92 (61.76-62.08)
Non-Chronic Prescription Use	59.34 (58.84-59.82)
Chronic Prescription Use	54.88 (53.23-56.52)
OUD/BUP	72.32 (69.54-75.10)
Contraceptive Method Type	
Any Method	61.66 (61.49-61.69)
Sterilization	13.26 (12.98-13.54)
LARC	76.58 (76.30-76.86)
Moderately Effective Methods	66.19 (65.99-66.39)
Age at Delivery	
>20	75.51 (74.64-76.38)
20-24	69.32 (68.90-69.74)
25-29	61.49 (61.23-61.76)
30-34	60.82 (60.56-61.08)
35-39	55.82 (55.41-56.23)
40+	50.54 (49,60-51.49)
Delivery Mode	
Vaginal	67.58 (67.39-67.78)
Cesarean	52.11 (51.86-52.35)
Non-Opioid Substance Use Disorder	
No	61.55 (61.39-61.70)
Yes	67.97 (66.56-69.37)

Covariates	Mean Days to Contraceptive Provision (95% CI)
Psychiatric Disorder, Any	
No	61.59 (61.43-61.75)
Yes	62.50 (61.85-63.15)
Chronic Hypertension	
No	62.21 (61.96-62.28)
Yes	56.76 (56.26-57.26)
Gestational Hypertension	
No	61.87 (61.71-62.04)
Yes	60.09 (59.67-60.50)
Diabetes Mellitus	
No	61.91 (61.75-62.06)
Yes	55.61 (54.85-56.37)
Gestational Diabetes	
No	62.26 (62.10-62.43)
Yes	57.97 (57.57-58.38)
Asthma	
No	61.65 (61.49-61.81)
Yes	61.47 (60.79-62.15)
Autoimmune Disease	
No	61.66 (61.50-61.81)
Yes	60.89 (59.75-62.04)
Pain Condition	
No	61.68 (61.52-61.84)
Yes	61.18 (60.63-61.74)
Hepatitis C	
No	61.64 (61.49-61.79)
Yes	63.37 (57.31-69.42)

An adjusted linear regression model was run to calculate the mean time to contraceptive provision by opioid use category, adjusted for all covariates including maternal age, HRSA region, state-level demographic characteristics, insurance plan type, year of delivery, delivery mode, and chronic conditions. The results of the linear regression, which was restricted to women with evidence of contraceptive provision within 365 days postpartum (N=638,018), are presented in Table 4.14 and Figure 4.6. In the adjusted analysis, women with no opioid use had an average time to contraceptive provision of 61.9 days (95% CI: 61.76-62.08). Women with non-chronic and chronic prescription opioid use had significantly shorter times to contraceptive provision (Non-Chronic Mean: 59.34 days, 95% CI: 58.86-59.81; Chronic Mean: 54.88 days,

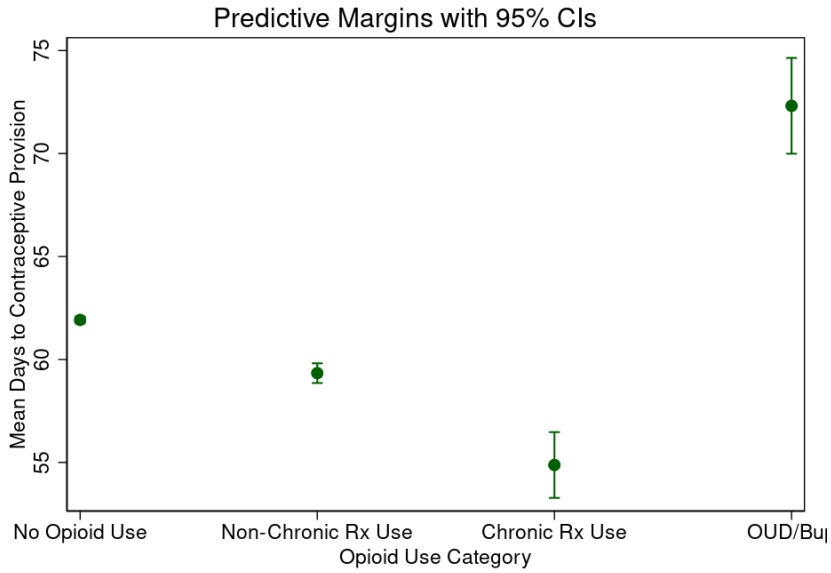
95% CI: 53.28-56.47). In contrast, women with OUD/Bup had a significantly longer time to contraceptive provision (Mean: 72.32, 95% CI: 69.99-74.64).

Table 4.14 Adjusted Mean Days to Contraceptive Provision and 95% CIs by Opioid-Use Among Women Provided Contraception Within 365 Days Postpartum*

Opioid Use Group	Adjusted Mean Days to Contraceptive Provision (95% CI)
No Use	61.92 (61.76-62.08)
Non-Chronic Use	59.34 (58.86-59.81)
Chronic Use	54.88 (53.28-56.47)
OUD/BUP	72.32 (69.99-74.64)

**Adjusted for: maternal age, HRSA region, state-characteristics, insurance plan type, delivery mode, year of delivery, opioid use category, non-opioid SUD, psychiatric diagnosis, chronic hypertension, gestational hypertension, diabetes, gestational diabetes, asthma, pain condition, autoimmune condition*

Figure 4.6 Adjusted Mean Days to Contraceptive provision and 95% CIs by Opioid-Use Among Women Provided Contraception Within 365 Days Postpartum



The next phase of the analysis involved estimating cumulative hazard and survival curves to visualize the overall pattern of contraceptive provision over the study period (Figures 4.7, 4.8). In both figures, there is a sharp increase in the hazard and number of "events" (e.g. contraceptive provision) around the 60-day postpartum timeframe. By approximately 200 days postpartum,

50% of women have received postpartum contraception; the slope of the survival function plateaued at roughly this point (Figure 4.8).

Figure 4.7 Nelson-Aalen Cumulative Hazard Estimate for Provision of Postpartum Contraception

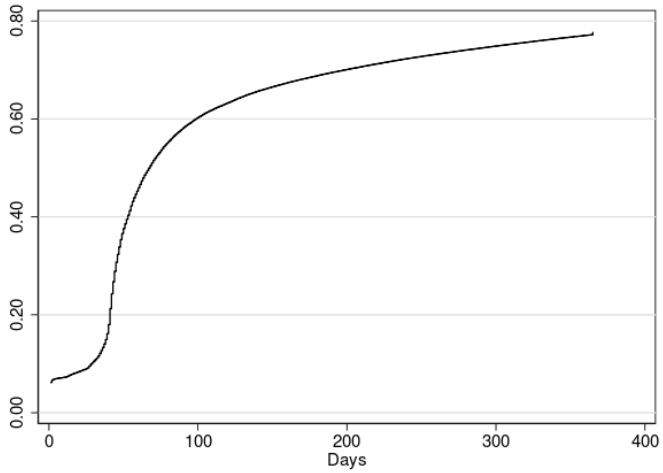
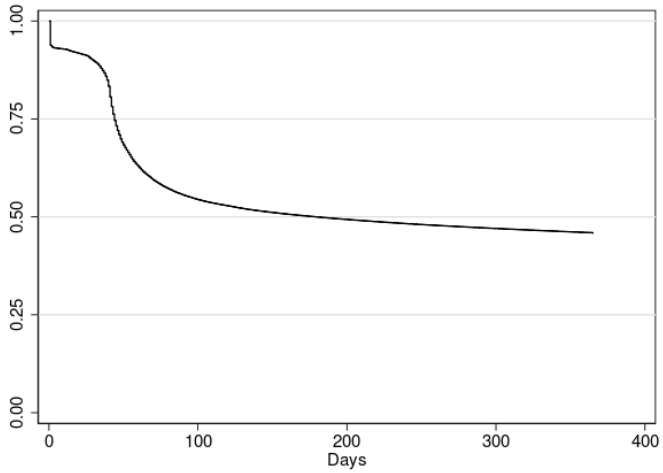


Figure 4.8 Kaplan-Meier Survival Estimate for Provision of Postpartum Contraception

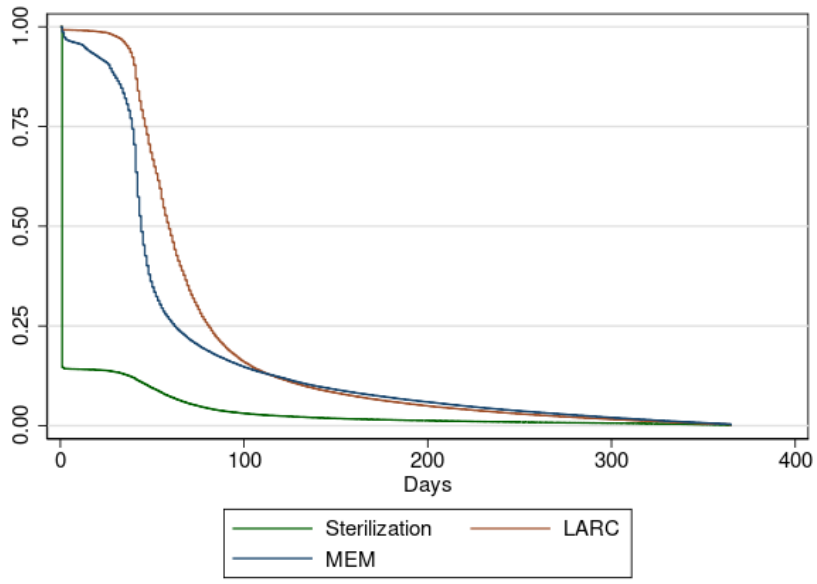


Kaplan-Meier curves for each categorical variable, including maternal age, year of delivery, HRSA region, state-level demographic characteristics, insurance plan type, delivery mode, and each comorbidity, were generated to assess the survival function for each category and provide a visual indication of whether the survival functions were proportional. Log rank

tests were then performed to formally test for equality across strata in each categorical variable, with a p-value<0.05 indicating that the survival function is different across strata. Log-log plots, which plot the log of the negative log of the survival function against log time, were also generated to examine the proportional hazards (PH) assumption for each categorical variable. If the PH assumption holds, the lines in the log-log plot should be parallel. Select Kaplan-Meier curves are included here. The full set of graphs for all categorical covariates can be found in Appendix E.

Among women who received contraception, the Kaplan-Meier curve demonstrated that sterilization occurred most frequently in the immediate postpartum period (Figure 4.9). MEM and LARC provision occurred later in the postpartum period, with rapid increases in provision occurring near the 60-day postpartum period. No log-rank test was performed for the Kaplan-Meier estimates by method of contraception as this variable was not included in the multivariable Cox model.

Figure 4.9 Kaplan-Meier Survival Estimate for Women Who Received Contraception During Study Period, by Contraceptive Method



The Kaplan-Meier curves by opioid use group and the accompanying log rank test demonstrated that the survival curves were not equal across strata (Figure 4.10, Table 4.15). Women with chronic prescription opioid use had an immediate and substantial drop, driven by the high levels of sterilization, which tended to occur immediately postpartum. All groups experienced an increase in contraceptive provision at approximately the 60-day mark, but the survival curve slopes are different. At approximately 100 days postpartum, the curves for the OUD/Bup group and non-use group cross-over, indicating a probable violation of the proportional hazards' assumption. The log-rank test yielded a p-value <<0.001 indicating that the survival functions for the different groups of opioid use during pregnancy were not equal (Table 4.15). The log rank tests for all other covariates, except autoimmune disease and hepatitis C, were significant ($p<0.05$). The full results of the log rank tests for all categorical covariates can be found in Appendix D.

Figure 4.10 Kaplan-Meier Survival Estimate by Type of Opioid Use

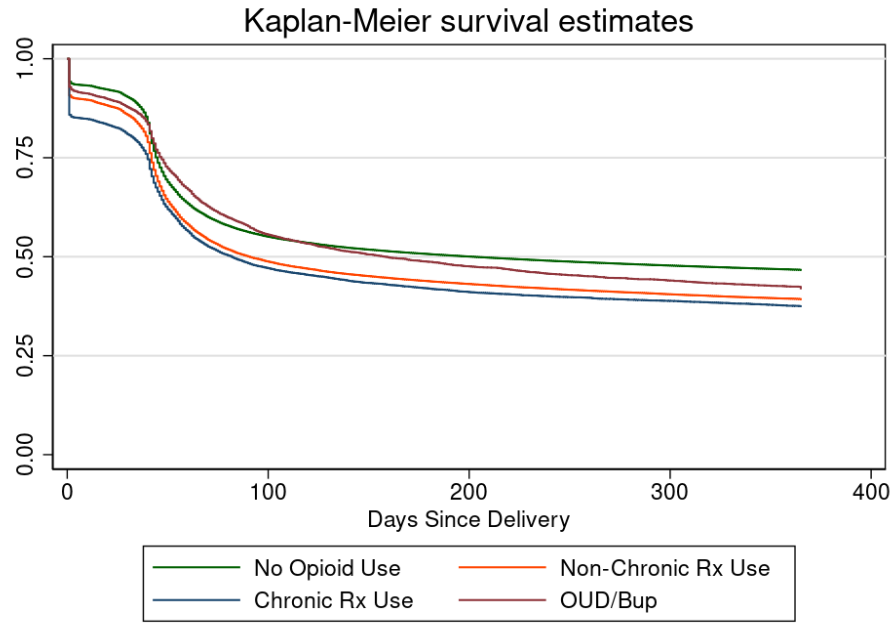


Table 4.15 Log-Rank Test Result from Kaplan-Meier Curves for Type of Opioid Use

Opioid Use Category	Events Observed	Events Expected	P-Value
No Opioid Use During Pregnancy	565,692	577,757.79	<0.001
Non-Chronic Prescription Opioid Use	63,919	53,233.95	
Chronic Prescription Opioid Use	5,713	4,432.52	
OUD/Buprenorphine	2,694	2,593.74	

Aim 2: Multivariable Cox Proportional Hazards Model Results

The unadjusted and adjusted results of the Cox Proportional Hazards models are presented in table 4.16. For the sake of brevity, the unadjusted results are discussed briefly and the adjusted model results are discussed at length below.

Table 4.16 Unadjusted and Adjusted Hazard Ratios for Any Prescription Contraceptive Provision (N=1,270,832); Time Period: Delivery-365 Days Postpartum

Variables	Unadjusted HR	Adjusted HR
Opioid Use		
No Opioid Use During Pregnancy	(ref.)	(ref.)
Non-Chronic Prescription Opioid Use	1.23 (1.22-1.24)***	1.15 (1.14-1.16)***
Chronic Prescription Opioid Use	1.32 (1.29-1.36)***	1.24 (1.21-1.27)***
OUD Diagnosis/Buprenorphine Prescription	1.06 (1.02-1.10)**	0.93 (0.89-0.97)**
Age		
<20	1.13 (1.11-1.14)***	1.14 (1.13-1.16)***
20-24	1.08 (1.07-1.09)***	1.07 (1.06-1.08)***
25-29	(ref.)	(ref.)
30-34	0.87 (0.87-0.88)***	0.89 (0.88-0.89)***
35-39	0.78 (0.77-0.78)***	0.78 (0.78-0.79)***
40+	0.64 (0.63-0.65)***	0.64 (0.63-0.65)***
HRSA Region		
Region 1	0.96 (0.95-0.97)***	1.00 (0.99-1.02)
Region 2	0.73 (0.72-0.74)***	0.78 (0.77-0.80)***
Region 3	(ref.)	(ref.)
Region 4	1.25 (1.24-1.26)***	1.20 (1.18-1.22)***
Region 5	1.03 (1.02-1.04)***	1.04 (1.02-1.05)***
Region 6	1.24 (1.22-1.25)***	1.26 (1.24-1.28)***
Region 7	1.20 (1.18-1.22)***	1.19 (1.17-1.21)***
Region 8	1.19 (1.18-1.21)***	1.27 (1.25-1.29)***
Region 9	0.92 (0.91-0.94)***	1.02 (1.00-1.04)*
Region 10	1.16 (1.14-1.18)***	1.19 (1.17-1.21)***
Unknown	1.12 (1.11-1.14)***	1.12 (1.10-1.14)***
Delivery in State with ≥20% Hispanic Population	0.93 (0.92-0.94)***	0.92 (0.91-0.93)***
Delivery in State with ≥20% Black Population	1.20 (1.19-1.21)***	1.02 (1.01-1.03)***

Delivery in State with ≥15% Population in Poverty	1.27 (1.26-1.28)***	1.06 (1.05-1.08)***
Delivery in State with ≥35% Women with College Degree or More	0.85 (0.84-0.86)***	0.99 (0.98-1.00)
Insurance Plan Type		
PPO	(ref.)	(ref.)
Comprehensive	0.99 (0.96-1.01)	0.98 (0.95-1.00)
HMO/EPO	0.99 (0.98-0.99)**	1.04 (1.03-1.05)***
POS/POS + Capitation	1.03 (1.02-1.04)***	1.01 (1.00-1.02)*
CDHP	1.01 (1.00-1.02)**	1.00 (0.99-1.01)
HDHP	0.91 (0.90-0.92)***	0.95 (0.94-0.96)***
Unknown	0.99 (0.97-1.00)	1.02 (1.00-1.03)*
Year of Delivery		
2011	(ref.)	(ref.)
2012	0.99 (0.99-1.00)	0.99 (0.98-1.00)
2013	1.02 (1.01-1.03)***	1.02 (1.01-.103)***
2014	0.98 (0.97-0.99)***	0.99 (0.98-0.99)**
2015	0.96 (0.95-0.97)***	0.94 (0.93-0.95)***
2016	0.92 (0.91-0.93)***	0.91 (0.90-0.92)***
Delivery Mode		
Vaginal	(ref.)	(ref.)
Cesarean	1.28 (1.27-1.28)***	1.30 (1.29-1.31)***
Non-Opioid Substance Use Disorder	1.11 (1.08-1.13)***	1.02 (0.99-1.04)
Psychiatric Disorder, Any	1.11 (1.10-1.12)***	1.10 (1.09-1.11)***
Chronic Hypertension	1.15 (1.14-1.16)***	1.09 (1.08-1.10)***
Gestational Hypertension	1.11 (1.10-1.12)***	1.00 (0.99-1.01)
Diabetes Mellitus	1.02 (1.00-1.03)*	1.01 (0.99-1.02)
Gestational Diabetes	0.99 (0.98-1.00)*	0.99 (0.98-1.00)
Asthma	1.10 (1.09-1.11)***	1.08 (1.07-1.10)***
Autoimmune Disease	0.99 (0.97-1.01)	-
Pain Condition	1.07 (1.06-1.08)***	1.03 (1.02-1.04)***
Hepatitis C	0.97 (0.89-1.06)	-

*p<0.05, **p<0.01, ***p<0.001

In the bivariate Cox regressions, the hazard of contraceptive provision was significantly higher for all categories of opioid use compared with women who did not use opioids during pregnancy (Table 4.16). Women with chronic prescription opioid use had the highest hazard of contraceptive provision (HR: 1.32, 95% CI: 1.29-1.36). The hazard of contraceptive provision decreased with age, with women in the oldest age groups significantly less likely to receive contraception than women aged 25-29. Women with a comorbidity had a higher hazard of contraceptive provision compared with women who did not across all comorbidities, except for gestational diabetes, autoimmune disease, and hepatitis C.

Variables that reached a significance level of $p<0.05$ in the bivariate analysis or variables with a known or theoretical association with postpartum contraception were included in the multivariable model. After adjustment, the association for the OUD/Bup group changed from an increased hazard in the bivariate analysis to a significantly decreased hazard in the multivariable model, compared to women who did not use opioids during pregnancy (Table 4.16). The direction of association for the non-chronic and chronic prescription opioid use groups did not change, although the magnitude of the hazard was attenuated.

The relationship between age and provision of contraception was unchanged after adjustment. Women in the youngest age groups had significantly higher hazard of contraceptive provision, while women in the oldest age groups (≥30 years) a significantly lower hazard, compared to the reference group of women aged 25-29. Several comorbidities were not significant in the multivariable model including non-opioid SUD, gestational hypertension, diabetes, and gestational diabetes. Psychiatric disorders, chronic hypertension, asthma, and pain conditions remained significant; women with these conditions had a higher hazard of contraceptive provision than those without the conditions.

A test of the proportion-hazards assumption for the multivariable Cox model was performed using Schoenfeld residual's test, which tests whether the Schoenfeld residuals for each variable included in the model has a non-zero slope. A non-zero slope, indicated by a p-value<0.05, suggests that a given variable violates the PH assumption. A global PH test was also performed on the full model. The results of the Schoenfeld residual's test and global test are displayed in Table 4.17. Virtually every variable in the model included at least one category that violated the PH assumption. The global test also indicated a violation of the PH assumption ($p<<0.001$). These violations of the PH assumption were due in part to the large Aim 2 sample

size as p-values are dependent on sample size, even a small departure from a zero slope may result in a significant p-value. However, in order to further assess the PH violations, an extensive sensitivity analysis was conducted.

Table 4.17 Rho and P-Values for Schoenfeld Residual Tests of Proportional Hazards for Multivariable Cox Model

Variable	Rho	P-Value
Opioid Use		
No Opioid Use During Pregnancy	Ref.	-
Non-Chronic Prescription Opioid Use	0.001	0.251
Chronic Prescription Opioid Use	-0.004	0.004
OUD Diagnosis/Buprenorphine Prescription	-0.004	0.001
Age		
<20	0.04	<0.001
20-24	0.04	<0.001
25-29	Ref.	-
30-34	-0.02	<0.001
35-39	-0.06	<0.001
40+	-0.05	<0.001
HRSA Region		
Region 1	0.006	<0.001
Region 2	0.023	<0.001
Region 3	Ref.	
Region 4	0.001	0.391
Region 5	-0.000	0.752
Region 6	-0.002	0.068
Region 7	-0.003	0.007
Region 8	-0.012	<0.001
Region 9	0.003	0.011
Region 10	-0.011	<0.001
Unknown	-0.002	0.195
Delivery in State with ≥20% Hispanic Population	-0.001	0.445
Delivery in State with ≥20% Black Population	0.000	0.976
Delivery in State with ≥15% Population in Poverty	-0.011	<0.001
Delivery in State with ≥35% Women with College Degree or More	0.011	<0.001
Insurance Plan Type		
PPO	Ref.	-
Comprehensive	-0.001	0.293
HMO/EPO	-0.010	<0.001
POS/POS + Capitation	0.003	0.011
CDHP	-0.001	0.542
HDHP	-0.000	0.708
Unknown	-0.007	<0.001
Year of Delivery		

Variable		Rho	P-Value
	2011	Ref.	-
	2012	-0.004	0.003
	2013	-0.015	<0.001
	2014	-0.016	<0.001
	2015	-0.012	<0.001
	2016	-0.013	<0.001
Delivery Mode			
	Vaginal	Ref.	-
	Cesarean	-0.108	<0.001
Non-Opioid Substance Use Disorder		0.002	0.138
Psychiatric Disorder, Any		0.012	<0.001
Chronic Hypertension		-0.007	<0.001
Gestational Hypertension		0.014	<0.001
Diabetes Mellitus		-0.007	<0.001
Gestational Diabetes		-0.008	<0.001
Asthma		0.003	0.011
Pain Condition		0.006	<0.001
Global Test			<0.001

Aim 2: Sensitivity Analyses

Two separate sensitivity analyses were conducted for Aim 2. The first analysis compared the cohort of women who met the inclusion criteria for Aim 2, those who did not meet the criteria, and the full cohort of women with a live birth during the study period. This sensitivity analysis was designed to detect possible selection bias during creation of the analytic sample. The second sensitivity analysis addressed the PH violations in the multivariable Cox models.

No major differences emerged between the women included in the Aim 2 analysis compared with those who were excluded. However, they were only compared on the covariates available at the time of delivery which did not include opioid use during pregnancy, comorbidities, or postpartum contraceptive provision. Among the covariates available for comparison, the groups were similar in age and geographic distribution, as well as for mode of delivery (Table 4.18).

Table 4.18 Sensitivity Analysis: Characteristics of Women with a Livebirth During Study Period (January 2011-December 2016), by Inclusion Criteria*

	Met Aim 2 Inclusion Criteria	Did Not Meet Aim 2 Inclusion Criteria	Full Sample with Live Birth
Total N's (%)	1,270,832 (53.7%)	1,096,031 (46.3%)	2,366,863 (100%)
Age, mean years (SD)	30.2 (5.5)	29.8 (5.5)	30.0 (5.5)
Age, Categorical			
<20	2.9% (37,089)	2.9% (31,416)	2.9% (68,505)
20-24	12.4% (158,131)	14.6% (159,817)	13.4% (317,948)
25-29	27.9% (354,483)	30.0% (328,577)	28.9% (683,060)
30-34	35.1% (445,584)	33.2% (363,425)	34.2% (809,009)
35-39	17.4% (221,526)	15.7% (172,067)	16.6% (393,593)
40+	4.2% (54,019)	3.7% (40,729)	4.0% (94,748)
HRSA Region			
Region 1	4.3% (55,254)	3.6% (39,995)	4.0% (95,249)
Region 2	7.3% (93,385)	9.2% (101,405)	8.2% (194,790)
Region 3	8.8% (111,322)	9.3% (101,672)	9.0% (212,994)
Region 4	20.9% (265,460)	19.7% (215,812)	20.3% (481,272)
Region 5	18.6% (236,731)	18.0% (197,274)	18.3% (434,005)
Region 6	13.3% (169,643)	13.5% (147,832)	13.4% (317,475)
Region 7	4.0% (51,232)	3.8% (42,073)	3.9% (93,305)
Region 8	3.2% (40,969)	2.9% (32,232)	3.1% (73,201)
Region 9	12.2% (154,906)	11.1% (121,650)	11.7% (276,556)
Region 10	3.9% (50,210)	3.3% (36,736)	3.7% (86,946)
Unknown	3.3% (41,720)	5.4% (59,350)	4.3% (101,070)
Delivery in State with ≥20% Hispanic Population	29.5% (374,670)	27.7% (303,131)	28.6% (677,801)
Delivery in State with ≥20% Black Population	15.9% (202,221)	15.6% (170,878)	15.8% (373,099)
Delivery in State with ≥15% Population in Poverty	13.1% (167,013)	14.4% (157,362)	13.7% (324,375)
Delivery in State with ≥35% Women with College Degree or More	10.0% (127,759)	9.0% (98,736)	9.6% (226,495)
Insurance Plan Type			
PPO	60.2% (764,813)	61.2% (670,765)	60.7% (1,435,578)
Comprehensive	0.9% (11,523)	0.9% (9,531)	0.9% (21,054)
HMO/EPO	14.9% (189,815)	13.9% (152,666)	14.5% (342,481)
POS/POS+Capitation	7.2% (92,110)	6.1% (66,940)	6.7% (159,050)
CDHP	7.5% (95,381)	5.7% (62,534)	6.7% (157,915)
HDHP	5.6% (71,385)	6.0% (65,902)	5.8% (137,287)
Unknown	3.6% (45,805)	6.2% (67,693)	4.8% (113,498)
Year of Delivery			
2011	22.2% (282,670)	19.1% (209,474)	20.8% (492,144)
2012	22.3% (283,552)	17.8% (195,595)	20.2% (479,147)
2013	16.2% (205,679)	15.3% (167,797)	15.8% (373,476)
2014	15.8% (201,057)	16.0% (174,891)	15.9% (375,948)
2015	11.9% (151,938)	6.6% (72,100)	9.5% (224,038)
2016	11.5% (145,936)	6.5% (71,655)	9.2% (217,591)
2017	N/A	18.7% (204,519)	8.6% (204,519)
Delivery Mode			
Vaginal	64.5% (819,145)	65.3% (715,851)	64.8% (1,534,996)

	Met Aim 2 Inclusion Criteria	Did Not Meet Aim 2 Inclusion Criteria	Full Sample with Live Birth
Cesarean	35.5% (451,687)	34.7% (380,180)	35.1% (831,867)

**Notes for Table 4.18: only variables measured at time of delivery are assessed because this table includes women who did not meet inclusion criteria and therefore, did not have prenatal/postpartum data consistently available.*

N/A= Not applicable; indicates a variable that was not included in the research aim

The second sensitivity analysis addressed the PH violations in the multivariable Cox model presented above. Three multivariable Cox models were run across three different follow up time periods to address the PH assumption violations. The first model (Model A) included the entire follow up period, from the date of delivery through 365 days postpartum and reflects the multivariable model presented in table 4.16. The second model (Model B) followed women from the date of delivery through the first 60 days postpartum. Model B included women who were provided contraception within 60 days postpartum, lost continuous coverage within 60 days postpartum, or were administratively censored at 60 days postpartum. The final model, Model C, included the period from 61 days postpartum through 365 days postpartum. Women included in Model C were those who maintained continuous coverage through at least 61 days postpartum but had not yet received postpartum contraception by that time. These timeframes were selected because in both the Kaplan-Meier curves and log-log plots, the 60-day mark consistently coincided with a large increase in contraceptive provision. The objective of running these three models was to estimate whether the direction of association between a given covariate and provision of contraception changed over the different time periods and what impact the conflicting hazard ratios had on the hazard ratio in Model A. This approach also helped illuminate changing patterns in contraceptive provision over the postpartum period.

Opioid use during pregnancy was the primary independent variable for which any potential PH violation was of concern. Among women with non-chronic and chronic

prescription opioid use during pregnancy, the relationship with postpartum contraceptive provision was consistent across all three models; they had a higher hazard of contraceptive provision in all models than women who did not use opioids during pregnancy (Table 4.19). The results for the OUD/Bup category, however, were not consistent across the models. In the first zero-60 days postpartum (Model B), women with OUD/Bup had a significantly lower hazard of contraceptive provision than women who did not use opioids during pregnancy. In Model C, covering 61-365 days postpartum, women in the OUD/Bup group who had not yet been provided contraception had a non-significant increased hazard of provision compared to women who did not use opioids during pregnancy and had yet to be provided contraception by 60 days postpartum. This change in association over the two time periods resulted in a significant but attenuated hazard ratio in Model A (aHR: 0.93, 95% CI: 0.89-0.97), weighted towards the decreased hazard results of Model B. This finding indicates that women in the OUD/Bup group had a lower hazard of provision of contraception in the early postpartum period, but after the first 60 days postpartum, there was no significant difference in the instantaneous risk of contraceptive provision between OUD/Bup and non-opioid users among women who had not received contraception by 60 days postpartum.

The age variable also displayed significant changes in the association across the three models. Although age and postpartum contraceptive provision was not the focus of this analysis, age is an important adjustment variable and the magnitude of difference across the models is worth noting. The direction of association was consistent for the three oldest age groups: 30-34, 35-39, and 40+, with each group having a significantly lower hazard of contraceptive provision in each model. Women in the two youngest age groups, <20 and 20-24, had a significantly lower hazard of contraception provision in the first 60 days postpartum than women aged 25-29 (Model

B), but in Model C, women aged <20 and 20-24 had a significantly increased hazard of contraceptive provision among women who had not received contraception by 60 days postpartum. Model A results were weighted towards the model C results, with women aged <20 (aHR: 1.14, 95% CI: 1.13-1.16) and 20-24 (aHR: 1.07, 95% CI: 1.06-1.08) having a significantly increased hazard of contraceptive provision.

There were several other variables that demonstrated a change in association across the three models including selected HRSA regions, delivering in a state with 35% or more of women with at least a college degree, years 2012-2014, mode of delivery, non-opioid SUD, gestational hypertension, diabetes, and gestational diabetes. These PH violations were of minimal concern because the analysis was not focused on the relationship between the covariates and postpartum contraceptive provision, rather, they were included to adjusted for potential confounding.

Table 4.19 Adjusted Hazard Ratios for Prescription Contraceptive Provision, Comparing Three Time Periods[‡]

Sample Size	**Model A N=1,270,832**	**Model B N=1,270,832**	**Model C N=742,035**
Opioid Use			
No Opioid Use During Pregnancy	(ref.)	(ref.)	(ref.)
Non-Chronic Prescription Opioid Use	1.15 (1.14-1.16)***	1.13 (1.12-1.14)***	1.19 (1.17-1.21)***
Chronic Prescription Opioid Use	1.24 (1.21-1.27)***	1.23 (1.19-1.27)***	1.27 (1.21-1.34)***
OUD Diagnosis/Buprenorphine Rx	*0.93 (0.89-0.97)***	*0.85 (0.81-0.90)****	*1.05 (0.99-1.13)*
Age			
<20	*1.14 (1.13-1.16)****	*0.95 (0.94-0.97)****	*1.65 (1.62-1.69)****
20-24	*1.07 (1.06-1.08)****	*0.97 (0.96-0.98)****	*1.35 (1.33-1.37)****
25-29	(ref.)	(ref.)	(ref.)
30-34	0.89 (0.88-0.89)***	0.91 (0.90-0.92)***	0.82 (0.81-0.83)***
35-39	0.78 (0.78-0.79)***	0.85 (0.84-0.86)***	0.65 (0.64-0.66)***
40+	0.64 (0.63-0.65)***	0.73 (0.72-0.74)***	0.47 (0.46-0.48)***
HRSA Region			
Region 1	*1.00 (0.99-1.02)*	*0.96 (0.94-0.98)****	*1.11 (1.08-1.14)****
Region 2	0.78 (0.77-0.80)***	0.73 (0.71-0.74)***	0.91 (0.89-0.93)***
Region 3	(ref.)	(ref.)	(ref.)
Region 4	1.20 (1.18-1.22)***	1.21 (1.18-1.23)***	1.18 (1.15-1.22)***
Region 5	*1.04 (1.02-1.05)****	*1.05 (1.04-1.07)****	*0.99 (0.97-1.01)*
Region 6	1.26 (1.24-1.28)***	1.30 (1.28-1.33)***	1.15 (1.11-1.19)***

	Model A	Model B	Model C
Region 7	1.19 (1.17-1.21)***	1.23 (1.21-1.25)***	1.08 (1.05-1.11)***
Region 8	1.27 (1.25-1.29)***	1.35 (1.32-1.37)***	1.06 (1.03-1.10)***
Region 9	*1.02 (1.00-1.04)**	*1.04 (1.01-1.06)***	*0.98 (0.94-1.01)*
Region 10	1.19 (1.17-1.21)***	1.25 (1.22-1.27)***	1.03 (1.01-1.07)*
Unknown	1.12 (1.10-1.14)***	1.12 (1.10-1.15)***	1.09 (1.05-1.12)***
Delivery in State with ≥20% Hispanic Population	0.92 (0.91-0.93)***	0.89 (0.88-0.91)***	0.97 (0.95-0.99)*
Delivery in State with ≥20% Black Population	1.02 (1.01-1.03)***	1.02 (1.00-1.03)*	1.04 (1.02-1.06)***
Delivery in State with ≥15% Population in Poverty	1.06 (1.05-1.08)***	1.08 (1.07-1.09)***	1.02 (0.99-1.04)
Delivery in State with ≥35% Women with College Degree or More	*0.99 (0.98-1.00)*	*0.96 (0.94-0.97)****	*1.04 (1.02-1.07)****
Insurance Plan Type			
PPO	(ref.)	(ref.)	(ref.)
Comprehensive	0.98 (0.95-1.00)	0.97 (0.94-1.01)	0.97 (0.93-1.02)
HMO/EPO	*1.04 (1.03-1.05)****	*1.06 (1.05-1.07)****	*0.99 (0.98-1.01)*
POS/POS + Capitation	1.01 (1.00-1.02)*	1.00 (0.99-1.01)	1.03 (1.02-1.05)***
CDHP	*1.00 (0.99-1.01)*	*1.01 (1.00-1.02)*	*0.98 (0.96-0.99)**
HDHP	0.95 (0.94-0.96)***	0.96 (0.94-0.97)***	0.95 (0.93-0.97)***
Unknown	*1.02 (1.00-1.03)**	*1.04 (1.03-1.06)****	*0.94 (0.91-0.97)****
Year of Delivery			
2011	(ref.)	(ref.)	(ref.)
2012	*0.99 (0.98-1.00)*	*1.01 (1.00-1.02)*	*0.96 (0.95-0.97)****
2013	*1.02 (1.01-.103)****	*1.06 (1.05-1.07)****	*0.93 (0.92-0.95)****
2014	*0.99 (0.98-0.99)***	*1.03 (1.02-1.04)****	*0.90 (0.88-0.91)****
2015	0.94 (0.93-0.95)***	0.98 (0.97-0.99)***	0.86 (0.85-0.88)***
2016	0.91 (0.90-0.92)***	0.95 (0.94-0.96)***	0.81 (0.79-0.82)***
Delivery Mode			
Vaginal	(ref.)	(ref.)	(ref.)
Cesarean	*1.30 (1.29-1.31)****	*1.43 (1.42-1.44)****	*1.00 (0.99-1.01)*
Non-Opioid Substance Use Disorder	*1.02 (0.99-1.04)*	*0.99 (0.97-1.02)*	*1.05 (1.01-1.09)**
Psychiatric Disorder, Any	1.10 (1.09-1.11)***	1.06 (1.04-1.07)***	1.21 (1.19-1.24)***
Chronic Hypertension	1.09 (1.08-1.10)***	1.09 (1.08-1.11)***	1.08 (1.06-1.10)***
Gestational Hypertension	*1.00 (0.99-1.01)*	*0.98 (0.97-0.99)****	*1.06 (1.05-1.08)****
Diabetes Mellitus	*1.01 (0.99-1.02)*	*1.02 (1.01-1.03)***	*0.97 (0.95-1.00)*
Gestational Diabetes	*0.99 (0.98-1.00)*	*1.00 (0.99-1.01)*	*0.97 (0.96-0.99)***
Asthma	1.08 (1.07-1.10)***	1.08 (1.06-1.09)***	1.11 (1.08-1.13)***
Pain Condition	1.03 (1.02-1.04)***	1.01 (1.00-1.02)*	1.08 (1.06-1.10)***

**p<0.05, **p<0.01, ***p<0.001*

ǂ *Italicized hazard ratios are those that change in direction of association across the presented models*

4.5 Aim 3 Results

The Aim 3 analysis was restricted to women with evidence of opioid use during pregnancy; the sample excluded women with no evidence of opioid use. Table 4.20 displays the descriptive characteristics of the Aim 3 cohort. The majority of live births were to women ages

30-34 and who lived in HRSA Region's 4, 5, and 6 which primarily include states in the South, Southwest, and Midwest. Approximately 3.0% of livebirths were to women with unknown geographic region. The majority of women were insured through a PPO plan type. Clinically, over 45% of women had a cesarean delivery and the most common comorbidity experienced during pregnancy was gestational diabetes, followed closely by gestational hypertension. Provision of prescription contraception was 41.6% by 60 days postpartum. Approximately 1% of infants born to women in the Aim 3 cohort were diagnosed with NAS and 13% were admitted to the NICU. The mean hospital length of stay for infants was 4.6 days.

The cohort for Aim 3 was substantially smaller and differed from the samples for Aims 1 and 2 across several key variables because Aim 3 included only women with evidence of opioid use. The average age of delivery was slightly older for Aim 3 compared with Aims 1 and 2, as noted by a slightly higher percentage of women in the Aim 3 cohort aged 30 years or older at the time of delivery. The distribution of livebirths across HRSA regions was similar for Aims 1-3, with the Aim 3 cohort having slightly less representation in the Northeast regions (HRSA Regions 1-3) and slightly more from the South and Midwest (HRSA Regions 6-8). The Aim 3 cohort had a higher prevalence of every comorbidity, with a pronounced increase in the proportion of women with non-opioid SUD, psychiatric diagnoses, and pain conditions. Postpartum contraceptive provision within 60 days postpartum was slightly higher in the Aim 3 cohort compared to Aim 1, with the major difference stemming from higher levels of female sterilization in the Aim 3 cohort.

Table 4.20 Descriptive Characteristics of Aim 3 Cohort, Column Totals

Variable	Aim 3 Cohort, % (N)
Total N	63,897
Opioid Use During Pregnancy	
Non-Chronic Prescription Use	89.8% (57,394)

Variable	Aim 3 Cohort, % (N)
Chronic Prescription Use	7.6% (4,875)
OUD Diagnosis/Bup Prescription	2.5% (1,628)
Age, mean years (SD)	31.3 (4.8)
Age, Categorical	
<20	0.4% (272)
20-24	6.9% (4,409)
25-29	28.9% (18,487)
30-34	38.1% (24,350)
35-39	20.5% (13,116)
40+	5.1% (3,263)
HRSA Region	
Region 1	3.6% (2,334)
Region 2	6.1% (3,909)
Region 3	6.3% (4,046)
Region 4	23.0% (14,687)
Region 5	19.0% (12,154)
Region 6	17.2% (11,005)
Region 7	4.8% (3,102)
Region 8	4.2% (2,665)
Region 9	8.0% (5,128)
Region 10	4.7% (3,007)
Unknown	2.9% (1,860)
Delivery in State with ≥20% Hispanic Population	30.3% (19,368)
Delivery in State with ≥20% Black Population	16.0% (10,213)
Delivery in State with ≥15% Population in Poverty	13.0% (8,307)
Delivery in State with ≥35% Women with College Degree or More	8.1% (5,190)
Insurance Plan Type	
PPO	62.1% (39,652)
Comprehensive	1.1% (681)
HMO/EPO	13.3% (8,486)
POS/POS+Capitation	7.7% (4,924)
CDHP	7.7% (4,892)
HDHP	5.0% (3,169)
Unknown	3.3% (2,093)
Year of Delivery	
2011	25.7% (16,456)
2012	22.8% (14,555)
2013	15.6% (9,974)
2014	13.5% (8,628)
2015	10.1% (6,452)
2016	8.6% (5,529)
2017	3.6% (2,303)
Delivery Mode	
Vaginal	53.4% (34,120)
Cesarean Section	46.6% (29,777)
Non-Opioid Substance Use Disorder	3.1% (1,965)
Any Psychiatric Diagnoses	9.7% (6,191)

Variable	Aim 3 Cohort, % (N)
Chronic Hypertension	12.6% (8,068)
Gestational Hypertension	17.2% (11,010)
Diabetes Mellitus	5.0% (3,017)
Gestational Diabetes	17.9% (11,431)
Asthma	6.9% (4,397)
Autoimmune Disease	3.3% (2,137)
Pain Condition	16.8% (10,754)
Hepatitis C	0.1% (86)
Any ANC	98.1% (62,699)
Postpartum Care Visit within 60 Days	50.4% (32,218)
Contraceptive provision within 60 Days Postpartum	
No Provision	58.3% (37,287)
Evidence of Provision	41.6% (26,610)
Sterilization	10.1% (6,478)
LARC	7.0% (4,468)
Moderately Effective Methods	24.5% (15,664)
NAS Diagnosis, Infant	1.3% (852)
NICU Admissions, Infant	13.0% (8,310)
Mean Hospital Length of Stay (Days), Infant	4.6 (8.8)

Approximately 90% of women in the Aim 3 cohort had evidence of non-chronic prescription use during pregnancy; 9.6% with chronic prescription opioid use; and 2.5% OUD/Bup use (Table 4.21). As with cohorts for Aims 1 and 2, women in the chronic prescription opioid group were the oldest and women in the OUD/Bup group, the youngest. Women who had cesarean delivery were more likely to have chronic prescription opioid use than women with vaginal deliveries. With the exception of hepatitis C, women with a given comorbidity had a higher prevalence of chronic prescription opioid use than women who did not have a comorbidity. Women with non-opioid SUD, a psychiatric diagnosis, autoimmune disease, and pain conditions had particularly high levels of chronic prescription opioid use. Over 50% of women with non-opioid SUD or with hepatitis C had OUD/Bup.

Table 4.21 Characteristics of Aim 3 Cohort, by Type of Opioid Use During Pregnancy, Row Totals

	Non-Chronic Prescription Use	Chronic Prescription Use	OUD/Buprenorphine
Total N (%)	57,394 (89.8%)	4,875 (9.6%)	1,628 (2.5%)
Age, mean years (SD)	31.3 (4.8)	32.2 (4.7)	30.4 (5.3)
Age, Categorical			
<20	87.1% (237)	2.2% (6)	10.7% (29)
20-24	90.7% (4,000)	4.6% (202)	4.7% (207)
25-29	91.0% (16,822)	6.7% (1,231)	2.3% (434)
30-34	89.5% (21,805)	8.1% (1,964)	2.4% (581)
35-39	88.8% (11,647)	8.8% (1,160)	2.4% (309)
40+	88.3% (2,883)	9.6% (312)	2.1% (68)
HRSA Region			
Region 1	90.6% (2,114)	5.8% (135)	3.6% (85)
Region 2	86.4% (3,377)	7.8% (307)	5.8% (225)
Region 3	88.1% (3,565)	8.3% (336)	3.6% (145)
Region 4	90.9% (13,348)	6.9% (1,022)	2.2% (317)
Region 5	88.7% (10,785)	8.5% (1,028)	2.8% (341)
Region 6	91.4% (10,061)	6.9% (764)	1.6% (180)
Region 7	91.4% (2,824)	7.7% (239)	1.3% (39)
Region 8	89.6% (2,389)	8.3% (222)	2.0% (54)
Region 9	89.5% (4,590)	8.5% (434)	2.0% (104)
Region 10	88.9% (2,674)	7.9% (238)	3.2% (95)
Unknown	89.6% (1,667)	8.1% (150)	2.3% (43)
Delivery in State with ≥20% Hispanic Population			
Yes	90.9% (17,613)	7.3% (1,410)	1.8% (345)
No	89.3% (39,781)	7.8% (3,465)	2.8% (1,283)
Delivery in State with ≥20% Black Population			
Yes	90.9% (9,285)	6.9% (711)	2.1% (217)
No	89.6% (48,109)	7.7% (4,164)	2.6% (1,411)
Delivery in State with ≥15% Population in Poverty			
Yes	89.5% (7,434)	7.6% (631)	2.9% (242)
No	89.9% (49,960)	7.6% (4,244)	2.5% (1,386)
Delivery in State with ≥35% Women with College Degree or More			
Yes	90.1% (4,674)	7.0% (365)	2.9% (151)
No	89.8% (52,720)	7.7% (4,510)	2.5% (1,477)
Insurance Plan Type			
PPO	89.5% (35,477)	7.9% (3,118)	2.7% (1,057)
Comprehensive	83.0% (565)	11.4% (78)	5.6% (38)
HMO/EPO	91.1% (7,728)	7.0% (594)	1.9% (164)
POS/POS+Capitation	90.3% (4,449)	6.9% (340)	2.7% (135)
CDHP	90.5% (4,426)	7.4% (361)	2.1% (105)
HDHP	91.0% (2,884)	6.8% (215)	2.2% (70)
Unknown	89.1% (1,865)	8.1% (169)	2.8% (59)
Year of Delivery			
2011	91.0% (14,974)	7.1% (1,177)	1.8% (305)
2012	90.2% (13,136)	7.6% (1,111)	2.1% (308)

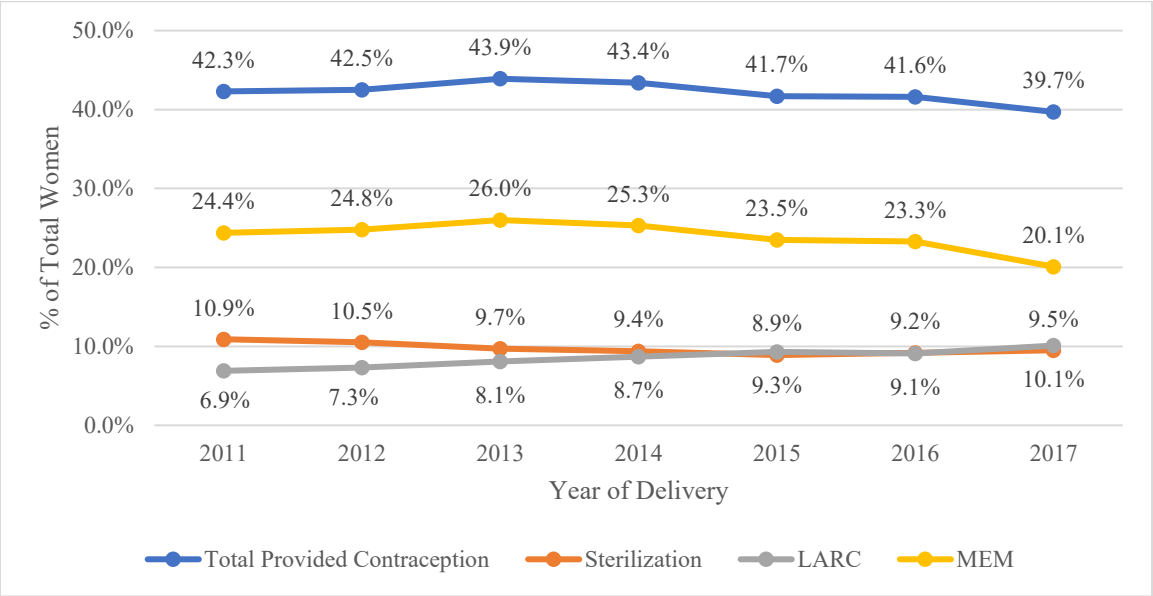
	Non-Chronic Prescription Use	Chronic Prescription Use	OUD/Buprenorphine
2013	90.0% (8,974)	7.7% (773)	2.3% (227)
2014	88.6% (7,641)	8.7% (748)	2.8% (239)
2015	88.4% (5,706)	8.0% (517)	3.5 (229)
2016	89.2% (4,930)	7.5% (413)	3.4% (186)
2017	88.3% (2,033)	5.9% (136)	5.8% (134)
Delivery Mode			
Vaginal	90.2% (30,773)	7.2% (2,460)	2.6% (887)
Cesarean	89.4% (26,621)	8.1% (2,415)	2.5% (741)
Non-Opioid Substance Use Disorder			
Yes	32.2% (632)	15.9% (312)	51.9% (1,021)
No	91.6% (56,762)	7.4% (4,563)	1.0% (607)
Any Psychiatric Diagnoses			
Yes	76.9% (4,762)	15.0% (927)	8.1% (502)
No	91.2% (52,632)	6.8% (3,948)	1.9% (1,126)
Chronic Hypertension			
Yes	86.0% (6,938)	11.0% (885)	3.0% (245)
No	90.4% (50,456)	7.1% (3,990)	2.5% (1,383)
Gestational Hypertension			
Yes	88.0% (9,693)	9.6% (1,057)	2.4% (260)
No	90.2% (47,701)	7.2% (3,818)	2.6% (1,368)
Diabetes Mellitus			
Yes	87.6% (3,407)	9.5% (368)	2.9% (114)
No	90.0% (53,987)	7.5% (4,507)	2.5% (1,514)
Gestational Diabetes			
Yes	89.9% (10,280)	8.2% (935)	1.9% (216)
No	89.8% (47,114)	7.5% (3,940)	2.7% (1,412)
Asthma			
Yes	87.2% (3,834)	10.0% (440)	2.8% (123)
No	90.0% (53,560)	7.4% (4,435)	2.5% (1,505)
Autoimmune Disease			
Yes	78.4% (1,675)	18.3% (391)	3.3% (71)
No	90.2% (55,719)	7.3% (4,484)	2.5% (1,557)
Pain Condition			
Yes	80.4% (8,643)	16.0% (1,723)	3.6% (388)
No	91.7% (48,751)	5.9% (3,152)	2.3% (1,240)
Hepatitis C			
Yes	38.4% (33)	4.6% (4)	57.0% (49)
No	89.9% (57,361)	7.6% (4,871)	2.5% (1,579)
Any ANC			
Yes	89.8% (56,307)	7.6% (4,797)	2.5% (1,595)
No	90.7% (1,087)	6.5% (78)	2.7% (33)
Postpartum Care Visit within 60 Days			
Yes	88.9% (28,638)	8.4% (2,716)	2.7% (864)

	Non-Chronic Prescription Use	Chronic Prescription Use	OUD/Buprenorphine
No	90.8% (28,765)	6.8% (2,159)	2.4% (764)
Provision of Prescription Contraceptive within 60 Days Postpartum			
No Evidence of Provision	90.0% (33,560)	7.2% (2,692)	2.8% (1,035)
Evidence of Provision	89.6% (23,834)	8.2% (2,183)	2.2% (593)
Sterilization	85.8% (5,556)	11.4% (736)	2.9% (186)
LARC	90.1% (4,028)	7.3% (327)	2.5% (113)
Moderately Effective Methods	91.0% (14,250)	7.1% (1,120)	1.9% (294)

Dependent Variable: Postpartum prescription Contraceptive Provision

The dependent variable in Aim 3 was provision of prescription contraception within 60 days postpartum, measured as a binary variable. In the Aim 3 cohort, 41.6% of women were provided prescription contraception within 60 days postpartum (Table 4.22), higher than the 37.6% of women in the Aim 1 cohort. This finding was expected as women with non-chronic and chronic prescription opioid use had higher levels of contraceptive provision within 60 days postpartum than women who did not use opioids during pregnancy. The trends in provision across the study period mirrored those observed in Aim 1 showing an overall decline in contraception provision, with sterilization declining (p for tend<0.00), LARC provision increasing (p for tend<0.00), and variable MEM provision, but declining in the final study year (Figure 4.11)

Figure 4.11 Trends for Provision of Prescription Contraception within 60 Days Postpartum, Overall and by Method Type, Aim 3 Cohort



Levels of contraceptive provision among the different categories of opioid use paralleled those in Aim 1, with contraceptive provision highest among women with chronic prescription opioid use and lowest in the OUD/Bup group. The covariates included in the Aim 3 analysis were explored using a binary measure of contraceptive provision rather than stratifying by method type due to a smaller number of observations in the sample. Patterns for contraceptive provision by age group and geographic region were similar to those in Aim 1. Contraceptive provision decreased with age. There was substantial regional variation in contraceptive provision by HRSA regions, ranging from a low of 30.4% in Region 2 (NY, NJ, PR) to a high of 46.2% in Region 8 (MT, ND, SD, WY, UT, CO). Contraceptive provision was variable across the different comorbidities: women with non-opioid SUD, diabetes, gestational diabetes, autoimmune disease, and hepatitis C has lower levels of contraceptive provision compared to some without these comorbidities. For the remaining comorbidities, including psychiatric diagnoses, chronic hypertension, gestational hypertension, asthma, and pain conditions, women

with the comorbidity had higher levels of contraceptive provision. Women with cesarean deliveries had substantially higher levels of contraceptive provision than women with vaginal deliveries, a trend observed across all three Aims. Women with a postpartum care visit within 60 days also had considerably higher levels of contraceptive provision than women with no postpartum visit.

Table 4.22 Characteristics of Aim 3 Cohort by Postpartum Contraceptive Provision within 60 Days of Delivery, Row Totals

	Not Provided Contraception	Provided Contraception
Total N	37,287 (58.3%)	26,610 (41.6%)
Opioid Use During Pregnancy		
Non-Chronic Prescription Use	58.5% (33,560)	41.5% (23,834)
Chronic Prescription Use	55.2% (2,692)	44.8% (2,183)
OUD Diagnosis/Bup Prescription	63.6% (1,035)	36.4% (593)
Age, mean years (SD)	31.6 (4.9)	31.0 (4.7)
Age, Categorical		
<20	57.7% (157)	42.3% (115)
20-24	54.5% (2,401)	45.5% (2,008)
25-29	54.9% (10,157)	45.1% (8,330)
30-34	58.8% (14,318)	41.2% (10,032)
35-39	61.8% (8,105)	38.2% (5,011)
40+	65.9% (2,149)	34.1% (1,114)
HRSA Region		
Region 1	65.5% (1,528)	34.5% (806)
Region 2	69.6% (2,722)	30.4% (1,187)
Region 3	63.8% (2,581)	36.2% (1,465)
Region 4	55.4% (8,137)	44.6% (6,550)
Region 5	59.5% (7,231)	40.5% (4,923)
Region 6	54.3% (6,001)	45.5% (5,004)
Region 7	54.5% (1,691)	45.5% (1,411)
Region 8	53.8% (1,433)	46.2% (1,232)
Region 9	63.7% (3,266)	36.3% (1,862)
Region 10	55.1% (1,657)	44.9% (1,350)
Unknown		44.1% (820)
Delivery in State with ≥20% Hispanic Population		
Yes	59.2% (11,470)	40.8% (7,898)
No	58.0% (25,817)	42.0% (18,712)
Delivery in State with ≥20% Black Population		
Yes	54.7% (5,589)	45.3% (4,624)
No	59.0% (31,698)	40.9% (21,986)
Delivery in State with ≥15% Population in Poverty		
Yes	53.2% (4,422)	46.8% (3,885)
No	59.1% (32,865)	40.9% (22,725)

	Not Provided Contraception	Provided Contraception
Delivery in State with ≥35% Women with College Degree or More		
Yes	66.1% (3,433)	33.8% (1,757)
No	57.7% (33,854)	42.3% (24,853)
Insurance Plan Type		
PPO	58.4% (23,161)	41.6% (16,491)
Comprehensive	55.6% (379)	44.3% (302)
HMO/EPO	58.4% (4,955)	41.6% (3,531)
POS/POS+Capitation	58.1% (2,859)	41.9% (2,065)
CDHP	57.1% (2,795)	42.9% (2,097)
HDHP	60.5% (1,918)	39.5% (1,251)
Unknown	58.3% (1,220)	41.7% (873)
Year of Delivery		
2011	58.5% (9,635)	41.4% (6,821)
2012	57.7% (8,406)	42.3% (6,149)
2013	57.0% (5,682)	43.0% (4,292)
2014	57.6% (4,971)	42.4% (3,657)
2015	59.9% (3,865)	40.1% (2,587)
2016	59.4% (3,284)	40.6% (2,245)
2017	62.7% (1,444)	37.3% (859)
Delivery Mode		
Vaginal	62.2% (21,231)	37.8% (12,889)
Cesarean	53.9% (16,056)	46.1% (13,721)
Non-Opioid Substance Use Disorder		
Yes	59.4% (1,168)	40.6% (797)
No	58.3% (36,119)	41.7% (25,813)
Any Psychiatric Diagnoses		
Yes	57.0% (3,529)	43.0% (2,662)
No	58.5% (33,758)	41.5% (23,948)
Chronic Hypertension		
Yes	55.4% (4,471)	44.6% (3,597)
No	58.8% (32,816)	41.2% (23,013)
Gestational Hypertension		
Yes	56.9% (6,262)	43.1% (4,748)
No	58.7% (31,025)	41.3% (21,862)
Diabetes Mellitus		
Yes	59.5% (2,315)	40.5% (1,574)
No	58.3% (34,972)	41.7% (25,036)
Gestational Diabetes		
Yes	58.8% (6,726)	41.2% (4,705)
No	58.2% (30,561)	41.7% (21,905)
Asthma		
Yes	57.0% (2,507)	43.0% (1,890)
No	58.4% (34,780)	41.5% (24,720)
Autoimmune Disease		
Yes	58.8% (1,256)	41.2% (881)
No	58.3% (36,031)	41.7% (25,729)

	Not Provided Contraception	Provided Contraception
Pain Condition		
Yes	56.7% (6,101)	43.3% (4,653)
No	58.7% (31,186)	41.3% (21,957)
Hepatitis C		
Yes	65.1% (56)	34.9% (30)
No	58.3% (37,231)	41.6% (26,580)
Any ANC		
Yes	58.4% (36,595)	41.6% (26,104)
No	57.7% (692)	42.2% (506)
Postpartum Care Visit within 60 Days		
Yes	52.2% (16,831)	47.8% (15,387)
No	64.6% (20,456)	35.4% (11,223)

Aim 3: Additional Exploratory Data Analysis

Inclusion of infant-level variables related to NAS, NICU admission, and hospital length of stay (LOS) required additional exploratory data analysis for the Aim 3 cohort. Cross-tabulations of the data were run to assess the distribution of opioid use and contraceptive methods across infant level variables. Of the 63,897 infant-mother dyads included in the analysis for Aim 3, 852 infants (1.3%) were diagnosed with non-iatrogenic NAS. Among infants with mothers in the OUD/Bup group, 27.8% were diagnosed with NAS, as were 5.2% of infants born to women with chronic prescription opioid use (Table 4.23). Approximately 13% of infants in the Aim 3 cohort were admitted to the NICU (n=8,310). Women in the OUD/Bup group were more likely to have infants admitted to the NICU (Table 4.23). The average infant hospital length of stay for the Aim 3 cohort was 4.6 days (SD: 8.8). Infants born to women in the OUD/Bup group had the longest average length of stay, while infants born to women with non-chronic prescription opioid use had the shortest stays, 30% shorter in length than infants born to women in the OUD/Bup group.

Table 4.23 Type of Opioid Use by Infant-Level Variables (N=63,897), Column Totals

	Type of Opioid Use		
NAS Diagnosis	**Non-Chronic Prescription**	**Chronic Prescription**	**OUD/Bup**
Yes	0.2% (146)	5.2% (254)	27.8% (452)
No	99.8% (57,248)	94.8% (4,621)	72.2% (1,176)
NICU Admission			
Yes	12.7% (7,320)	14.3% (697)	18.0% (293)
No	87.2% (50,074)	85.7% (4,178)	82.0% (1,335)
Infant Hospital LOS (mean, SD)	4.5 (8.8)	4.8 (8.6)	6.5 (9.5)

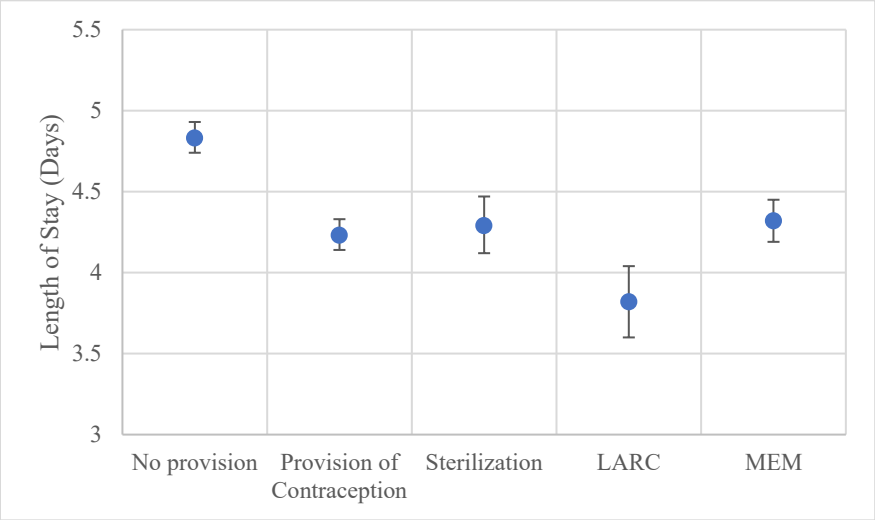
Contraceptive provision differed significantly by the infant variables (Table 4.24). Women whose infants were diagnosed with NAS had substantially lower levels of contraceptive provision than women whose infants did not have NAS (35.3% vs 41.7%) (Table 4.24). Despite the lower overall levels of contraceptive provision, sterilization was higher among women with infants diagnosed with NAS, while LARC and MEM provision was lower. Women with infants admitted to the NICU for any length of time also had lower levels of contraceptive provision, overall and for all method types. Infant hospital LOS varied significantly for women who were and were not provided contraception. Among women provided contraception, the average hospital length of stay for their infants was 4.2 days (95% CI: 4.13-4.32)) compared with 4.8 days (95% CI: 4.74-9.93) for women who were not provided contraception (Figure 4.12; Table 4.24). Women ultimately provided LARC had infants with the shortest average LOS (3.8 days, 95% CI: 3.60-4.04).

Table 4.24 Method of Prescription Contraception Provided within 60 Days Postpartum by Infant Variables (N=63,897), Row Totals

Infant Variable, % (N)	No Provision	Provided Contraception	Sterilization	LARC	Moderately Effective Methods
NAS Diagnosis					
Yes	64.7% (551)	35.3% (301)	13.1% (112)	5.0% (43)	17.1% (146)
No	58.3% (36,736)	41.7% (26,309)	10.1% (6,366)	7.0% (4,425)	24.6% (15,518)
NICU Admission					
Yes	61.0% (5,070)	39.0% (3,240)	9.8% (815)	6.1% (509)	23.1% (1,916)
No	57.9% (32,217)	42.0% (23,370)	10.2% (5,663)	7.1% (3,959)	24.7% (13,748)

Infant Hospital LOS (mean, 95% CI)	4.8 (4.74-9.93)	4.2 (4.13-4.32)	4.3 (4.12-4.47)	3.8 (3.60-4.04)	4.3 (4.19-4.45)

Figure 4.12 Average Infant Hospital Length of Stay (Mean, 95% CI) by Contraceptive Method Type



Severity of the NAS diagnosis was also explored in relation to contraceptive provision. A table of contraceptive method type stratified by NAS diagnosis and NICU admission was created to assess if levels contraceptive provision changed across strata of NAS diagnosis and NICU admission (Table 4.25). Women with infants who were both admitted to the NICU and had an NAS diagnosis had the lowest overall levels of contraceptive provision, particularly the lowest levels of LARC and MEM provision. In contrast, women with infants who had neither an NAS diagnosis nor an admission to the NICU had the highest levels of contraceptive provision, including for LARC and MEM.

Table 4.25 Contraceptive Method Provided within 60 Days Postpartum by Infant NAS Status and NICU Admission, Column Totals

	NAS Diagnosis in Infant (N=852)		No NAS Diagnosis in Infant (N=63,045)	
Contraceptive Method Type	Admitted to NICU (N=243)	Not Admitted to NICU (N=609)	Admitted to NICU (N=8,067)	Not Admitted to NICU (N=54,978)

No Provision	69.1% (168)	62.9% (383)	60.8% (4,902)	57.9% (31,834)
Provided Contraception	30.8% (75)	37.1% (226)	39.2% (3,165)	42.1% (23,144)
Sterilization	11.5% (28)	13.8% (84)	9.8% (787)	10.1% (5,579)
LARC	4.9% (12)	5.1% (31)	6.2% (497)	7.1% (3,928)
Moderately Effective Methods	14.4% (35)	18.2 (111)	23.3% (1,881)	24.9% (13,637)

Aim 3: Logistic Regression Models, Unadjusted and Adjusted

The unadjusted and adjusted odds of contraceptive provision within 60 days postpartum are presented in Table 4.26. Insurance plan type, hepatitis C, and any ANC were not included in the multivariable model because they were not significant ($p<0.05$) in the bivariate analysis and did not have a compelling theoretical reason for remaining in the multivariable model. The relationship between type of opioid use during pregnancy and contraceptive provision in the adjusted model was consistent with the findings in the unadjusted model. Women with chronic prescription use had increased odds of contraceptive provision (aOR: 1.11, 95% CI: 1.05-1.18) whereas women with OUD/Bup had decreased odds (aOR: 0.83, 95% CI: 0.72-0.94) compared to women with non-chronic prescription opioid use. NAS diagnosis and NICU admission for the infant were no longer significant after adjustment for confounders but the relationship between hospital LOS and contraceptive provision not only remained significant but increased in magnitude (aOR: 0.989, 95% CI: 0.986-0.991). The relationship between age and contraceptive provision was unchanged from the unadjusted model, with the odds of provision decreasing with increasing age. Women with cesarean deliveries were significantly more likely to receive contraception than women with vaginal deliveries in both the adjusted and unadjusted models.

Women in HRSA regions 4, 6-8, 10, (South, Southwest, West) and those from an unknown region had significantly higher odds of contraceptive provision than women in Region

3 (reference- PA, MD, DE, VA, WV). Women who delivered in states with 20% or more Hispanic population or in a state where 35% of more of women had a least a college degree had significantly lower odds of contraceptive provision. Women delivering in states with 20% or more Black population or states with 15% or more of the population in poverty had significantly higher odds of contraceptive provision. Among the chronic conditions, women with a psychiatric diagnosis or chronic hypertension had significantly increased odds of provision while women with diabetes had significantly lower odds of contraceptive provision compared to women without those conditions. Non-opioid SUD, gestational diabetes, asthma, and autoimmune disease remained non-significant in the adjusted model; gestational hypertension and pain conditions became non-significantly in the multivariable model. Finally, a postpartum care visit within 60 days continued to be significantly associated with provision of contraception (aOR: 1.64, 95% CI: 1.59-1.69).

Table 4.26 Unadjusted and Adjusted Odds of Any Prescription Contraceptive Provision within 60 Days Postpartum Among Women Who used Opioids During Pregnancy (N=63,897)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Opioid Use During Pregnancy		
Non-Chronic Prescription Use	(ref.)	(ref.)
Chronic Prescription Use	1.14 (1.08-1.21)***	1.11 (1.05-1.18)***
OUD Diagnosis/Bup Prescription	0.81 (0.73-0.89)***	0.83 (0.72-0.94)*
Age		
<20	0.89 (0.70-1.14)	0.98 (0.77-1.26)
20-24	1.02 (0.95-1.09)	1.05 (0.98-1.12)
25-29	(ref.)	(ref.)
30-34	0.85 (0.82-0.89)***	0.86 (0.82-0.89)***
35-39	0.75 (0.72-0.79)***	0.75 (0.71-0.79)***
40+	0.63 (0.58-0.68)***	0.62 (0.57-0.67)***
HRSA Region		
Region 1	0.93 (0.83-1.03)	1.01 (0.90-1.14)
Region 2	0.77 (0.70-0.84)***	0.79 (0.71-0.87)***
Region 3	(ref.)	(ref.)
Region 4	1.42 (1.32-1.52)***	1.17 (1.04-1.30)**
Region 5	1.20 (1.11-1.29)***	1.07 (0.99-1.16)
Region 6	1.47 (1.36-1.58)***	1.43 (1.26-1.61)***
Region 7	1.47 (1.34-1.62)***	1.33 (1.20-1.48)***
Region 8	1.52 (1.37-1.67)***	1.52 (1.37-1.69)***

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Region 9	1.00 (0.92-1.09)	1.05 (0.92-1.20)
Region 10	1.43 (1.30-1.58)***	1.29 (1.16-1.43)***
Unknown	1.39 (1.24-1.55)***	1.27 (1.13-1.43)***
Delivery in State with ≥20% Hispanic Population	0.95 (0.92-0.98)**	0.88 (0.81-0.97)**
Delivery in State with ≥20% Black Population	1.19 (1.14-1.24)***	1.09 (1.01-1.17)*
Delivery in State with ≥15% Population in Poverty	1.27 (1.21-1.33)***	1.08 (1.01-1.16)*
Delivery in State with ≥35% Women with College Degree or More	0.70 (0.66-0.74)***	0.84 (0.76-0.92)***
Insurance Plan Type		N/A
PPO	(ref.)	
Comprehensive	1.12 (0.96-1.30)	
HMO/EPO	1.00 (0.95-1.05)	
POS/POS+Capitation	1.01 (0.95-1.08)	
CDHP	1.05 (0.99-1.12)	
HDHP	0.92 (0.85-0.99)*	
Unknown	1.00 (0.92-1.10)	
Year of Delivery		
2011	(ref.)	(ref.)
2012	1.03 (0.99-1.08)	1.04 (0.99-1.09)
2013	1.07 (1.01-1.12)*	1.09 (1.04-1.15)**
2014	1.04 (0.98-1.09)	1.07 (1.01-1.13)*
2015	0.94 (0.89-1.00)	0.97 (0.91-1.03)
2016	0.96 (0.91-1.03)	0.98 (0.91-1.04)
2017	0.84 (0.77-0.92)***	0.84 (0.77-0.93)***
Delivery Mode		
Vaginal	(ref.)	(ref.)
Cesarean	1.41 (1.36-1.45)***	1.54 (1.49-1.59)***
Non-Opioid Substance Use Disorder	0.95 (0.87-1.05)	1.06 (0.95-1.19)
Any Psychiatric Diagnoses	1.06 (1.01-1.12)*	1.06 (1.01-1.13)*
Chronic Hypertension	1.15 (1.09-1.20)***	1.11 (1.06-1.18)***
Gestational Hypertension	1.08 (1.03-1.12)**	0.96 (0.92-1.01)
Diabetes Mellitus	0.95 (0.89-1.01)	0.92 (0.86-0.99)*
Gestational Diabetes	0.97 (0.94-1.02)	0.96 (0.92-1.00)
Asthma	1.06 (1.00-1.13)	1.05 (0.99-1.12)
Autoimmune Disease	0.98 (0.90-1.07)	0.97 (0.89-1.06)
Pain Condition	1.08 (1.04-1.13)***	1.04 (1.00-1.09)
Hepatitis C	0.75 (0.48-1.17)	N/A
Any ANC	0.97 (0.87-1.09)	N/A
Postpartum Care Visit within 60 Days	1.67 (1.61-1.72)***	1.64 (1.59-1.69)***
NAS Diagnosis, Infant	0.76 (0.66-0.89)***	0.86 (0.74-1.01)
NICU Admission, Infant	0.88 (0.84-0.92)***	0.95 (0.90-1.00)
Mean Hospital Length of Stay in Days, Infant	0.992 (0.990-0.994)***	0.989 (0.986-0.991)***

*p<0.05, **p<0.01, ***p<0.001
N/A= not applicable, covariate was not included in the model

Aim 3: Sensitivity Analysis

A sensitivity analysis was conducted comparing the characteristics of women who were successfully linked with an infant record and included in the Aim 3 analysis to those of women who were not linked with an infant, and the full sample of women who used opioids during pregnancy from the Aim 1 cohort (Table 4.27). An assessment of the magnitude and direction of potential selection bias in the Aim 3 cohort was assessed using the relative risk ratio (ROR). The aim of this sensitivity analysis was to understand differences among the three groups and how they may impact the interpretation of the Aim 3 results.

Overall, 51.5% of women who used opioids during pregnancy from the Aim 1 cohort were successfully linked with an infant record. Important differences emerged between women who were and were not included in the Aim 3 analysis. The linkage rates were different across the three types of opioid use: 52.3% of women with non-chronic prescription use were linked (57,394 linked/109,622 total); 52.1% of women with chronic prescription use were linked (4,875 linked/9,347 total); but only 31.6% of women with OUD/Bup were linked with their newborn (1,628 linked/5,155 total). It is not known why women in the OUD/Bup category had significantly lower linkage levels than women in the other opioid use categories.

Women included in the Aim 3 analysis were older, less likely to live in a state with a high proportion of Black residents or a state with a high poverty rate and had a different comorbidity profile than the women excluded from the analysis. Importantly, the fact that women with OUD/Bup were less likely to be included in the Aim 3 analysis may have impacted the infant-related variables, specifically infants diagnosed with NAS; the number with this diagnosis is likely underestimated as a result. Women with a non-opioid SUD, a psychiatric diagnosis, diabetes, asthma, pain condition, or hepatitis C were also less likely to be included in the Aim 3

analysis. These conditions, except for asthma and diabetes, also occur more frequently in women with OUD/Bup. Hypertension, gestational hypertension, gestational diabetes, and autoimmune disease were more common among women included in the Aim 3 analysis compared with excluded women. Despite these differences, there was only slight variation in the levels of contraceptive provision across the three groups, both overall and by method type. Women included in the Aim 3 analysis had lower levels of LARC provision, but comparable levels of sterilization and MEM compared to excluded women.

Table 4.27 Sensitivity Analysis: Characteristics of Women Included and Excluded from Aim 3 Cohort

	Linked with Infant	Not Linked with Infant	All Women with Opioid Use During Pregnancy from Aim 1
Total N (%)	63,897 (51.5%)	60,227 (48.5%)	124,124 (100%)
Opioid Use During Pregnancy			
Non-Chronic Prescription Use	89.8% (57,394)	86.7% (52,228)	88.3% (109,622)
Chronic Prescription Use	7.6% (4,875)	7.4% (4,472)	7.5% (9,347)
OUD Diagnosis/Bup Prescription	2.5% (1,628)	5.9% (3,527)	4.1% (5,155)
Age, mean years (SD)	31.3 (4.8)	28.5 (6.2)	30.0 (5.7)
Age, Categorical			
<20	0.4% (272)	6.4% (3,862)	3.3% (4,134)
20-24	6.9% (4,409)	24.4% (14,681)	15.4% (19,090)
25-29	28.9% (18,487)	24.9% (14,971)	26.9% (33,458)
30-34	38.1% (24,350)	26.0% (15,641)	32.2% (39,991)
35-39	20.5% (13,116)	14.2% (8,570)	17.5% (21,686)
40+	5.1% (3,263)	4.1% (2,502)	4.6% (5,765)
HRSA Region			
Region 1	3.6% (2,334)	2.7% (1,642)	3.2% (3,976)
Region 2	6.1% (3,909)	2.6% (1,570)	4.4% (5,479)
Region 3	6.3% (4,046)	9.1% (5,461)	7.7% (9,507)
Region 4	23.0% (14,687)	28.1% (16,925)	25.5% (31,612)
Region 5	19.0% (12,154)	14.9% (9,012)	17.0% (21,166)
Region 6	17.2% (11,005)	14.0% (8,454)	15.7% (19,459)
Region 7	4.8% (3,102)	3.6% (2,200)	4.3% (5,302)
Region 8	4.2% (2,665)	2.3% (1,412)	3.3% (4,077)
Region 9	8.0% (5,128)	16.0% (9,665)	11.9% (14,793)
Region 10	4.7% (3,007)	3.0% (1,810)	3.9% (4,817)
Unknown	2.9% (1,860)	3.4% (2,076)	3.2% (3,936)
Delivery in State with ≥20% Hispanic Population	30.3% (19,368)	31.2% (18,809)	30.8% (38,177)
Delivery in State with ≥20% Black Population	16.0% (10,213)	22.9% (13,811)	19.3% (24,024)
Delivery in State with ≥15% Population in Poverty	13.0% (8,307)	19.0% (11,437)	15.9% (19,744)

	Linked with Infant	Not Linked with Infant	All Women with Opioid Use During Pregnancy from Aim 1
Delivery in State with ≥35% Women with College Degree or More	8.1% (5,190)	8.4% (5,054)	8.2% (10,244)
Insurance Plan Type			
PPO	62.1% (39,652)	58.3% (35,108)	60.2% (74,760)
Comprehensive	1.1% (681)	1.3% (772)	1.2% (1,453)
HMO/EPO	13.3% (8,486)	18.0% (10,839)	15.6% (19,325)
POS/POS+Capitation	7.7% (4,924)	7.4% (4,450)	7.5% (9,374)
CDHP	7.7% (4,892)	7.6% (4,568)	7.6% (9,460)
HDHP	5.0% (3,169)	4.6% (2,748)	4.8% (5,917)
Unknown	3.3% (2,093)	2.9% (1,742)	3.1% (3,835)
Year of Delivery			
2011	25.7% (16,456)	23.0% (13,859)	24.4% (30,315)
2012	22.8% (14,555)	22.0% (13,259)	22.4% (27,814)
2013	15.6% (9,974)	16.7% (10,079)	16.2% (20,053)
2014	13.5% (8,628)	15.0% (9,067)	14.3% (17,695)
2015	10.1% (6,452)	10.4% (6,257)	10.2% (12,709)
2016	8.6% (5,529)	9.0% (5,453)	8.8% (10,982)
2017	3.6% (2,303)	3.7% (2,253)	3.7% (4,556)
Delivery Mode			
Vaginal	53.4% (34,120)	59.3% (35,740)	56.3% (69,860)
Cesarean	46.6% (29,777)	40.7% (24,487)	43.7% (54,264)
Non-Opioid Substance Use Disorder	3.1% (1,965)	7.2% (4,320)	5.1% (6,285)
Any Psychiatric Diagnoses	9.7% (6,191)	11.3% (6,792)	10.5% (12,983)
Chronic Hypertension	12.6% (8,068)	11.3% (6,815)	12.0% (14,883)
Gestational Hypertension	17.2% (11,010)	14.7% (8,889)	16.0% (19,899)
Diabetes Mellitus	5.0% (3,017)	6.1% (3,889)	5.6% (6,906)
Gestational Diabetes	17.9% (11,431)	14.8% (8,912)	16.4% (20,343)
Asthma	6.9% (4,397)	7.7% (4,620)	7.3% (9,017)
Autoimmune Disease	3.3% (2,137)	2.8% (1,680)	3.1% (3,817)
Pain Condition	16.8% (10,754)	17.3% (10,451)	17.1% (21,205)
Hepatitis C	0.1% (86)	0.5% (306)	0.3% (392)
Any ANC	98.1% (62,699)	96.6% (58,183)	97.4% (120,882)
Postpartum Care Visit within 60 Days	50.4% (32,218)	50.8% (30,571)	50.6% (62,789)
Contraceptive provision within 60 Days Postpartum			
No Provision	58.3% (37,287)	56.5% (34,050)	57.5% (71,337)
Evidence of Provision	41.6% (26,610)	43.5% (26,177)	42.5% (52,787)
Sterilization	10.1% (6,478)	9.9% (5,946)	10.0% (12,424)
LARC	7.0% (4,468)	9.0% (5,445)	8.0% (9,913)
Moderately Effective Methods	24.5% (15,664)	24.5% (14,786)	24.5% (30,450)

The magnitude and direction of potential selection bias in the Aim 3 cohort was evaluated using the relative odds ratio (ROR). A ROR equal to 1 suggests no differential selection bias; a

ROR>1 indicates an overestimation of the true association between the exposure and outcome in the subpopulation compared to the source population; a ROR<1 indicates an underestimation. The resulting ROR can be used as a selection-bias adjustment factor by multiplying the ROR by the subpopulation odds ratio.

Tables 4.28 and 4.29 show the number of women from the OUD/Bup and Non-chronic prescription opioid groups who received and did not receive postpartum contraception in the cohorts for Aim 1 and 3, respectively. The crude odds ratio, comparing the odds of postpartum contraceptive provision for women with OUD/Bup to women with non-chronic prescription opioid use, was 0.700 for Aim 1 and 0.808 for Aim 3. The resulting ROR of 1.15 indicated a positive (overestimation) bias of the true association between opioid use group and postpartum prescription contraception provision in the Aim 3 cohort. Multiplying the Aim 3 OR by a factor of 1.15 results in a ROR-adjusted OR of 0.93, indicating that after adjustment for possible selection bias, women with OUD/Bup have an attenuated but lower odds of contraceptive provision than women with non-chronic prescription opioid use. The ROR-adjusted OR of 0.93 is closer to the adjusted OR in main Aim 3 multivariable analysis (Table 4.26) of 0.87 (95% CI: 0.77-0.97).

Based on this ROR analysis, selection bias appears to have affected the results of Aim 3: either women with non-chronic prescription opioid use who were more likely to receive postpartum contraception were also more likely to be linked with an infant or women with OUD/Bup who were less likely to receive postpartum contraception were also more likely to be linked with an infant, resulting in the overestimation of the association observed in Aim 3. Although the magnitude of the relationship between OUD/Bup and contraceptive provision was likely overestimated in the Aim 3 results, women with OUD/Bup were still less likely to receive

postpartum prescription contraception compared to women with non-chronic prescription opioid use. The results of the ROR analysis do not offer insight into possible bias related to the infant level variables, therefore, it is possible that relationships observed between the infant variables and postpartum contraceptive provision are also subject to over or underestimation. Because there was no available source population with linked infant variables to compare the Aim 3 cohort to, an additional ROR analysis for the infant variables was not possible.

Table 4.28 Sensitivity Analysis: Crude Odds Ratio of Contraceptive Provision within 60 Days Postpartum for Aim 1 Cohort*

	Provided Contraception	**No Contraceptive Provision**	**Crude OR**
OUD/Bup	1,769	3,386	0.700
Non-chronic Prescription Opioid Use	46,859	62,763	

*Aim 1 numbers are from table 4.4.

Table 4.29 Sensitivity Analysis: Crude Odds Ratio of Contraceptive Provision within 60 Days Postpartum for Aim 3 Cohort*

	Provided Contraception	**No Contraceptive Provision**	**Crude OR**
OUD/Bup	593	1,035	0.808
Non-chronic Prescription Opioid Use	23,834	33,560	

*Aim 3 numbers are from table 4.22

4.6 Summary of Results

Overall, the results of this study consistently indicate that women with non-chronic and chronic prescription opioid use were significantly more likely to receive prescription contraception over the postpartum period while women with OUD/Bup were significantly less likely to receive prescription contraception than women who did not use opioids during pregnancy. This result was consistent across all the study Aims. In the Aim 1 analysis, women with non-chronic and chronic prescription opioid use were significantly more likely to receive

postpartum prescription contraception by 60 days postpartum and women with OUD/Bup were significantly less likely to receive postpartum contraception than women who did not use opioids. In an analysis by contraceptive method type, women with each type of opioid use during pregnancy had a significantly higher relative risk of receiving sterilization relative to no prescription method compared with women who did not use opioids during pregnancy.

Aim 2 examined contraceptive provision within 365 days postpartum. Women with OUD/Bup had the longest average time to contraceptive provision and women with chronic prescription opioid use had the shortest time to contraceptive provision among all women provided contraception in the Aim 2 cohort. In adjusted models, a similar pattern of contraceptive provision emerged: women with non-chronic and chronic prescription opioid use had a significantly increased hazard of contraceptive provision while women with OUD/Bup had a significantly lower hazard of provision compared to women who did not use opioids. An extensive sensitivity analysis highlighted the need for a nuanced approach in understanding contraceptive provision over the first year postpartum as the pattern of provision changed overtime for women with OUD/Bup compared to women who did not use opioids.

The Aim 3 analysis was restricted to women with evidence of opioid use during pregnancy. In adjusted models, increasing infant hospital length of stay was significantly associated with decreased provision of prescription contraception by 60 days postpartum, but NAS diagnosis and NICU admission were not associated with contraceptive provision. Women who were not provided contraception by 60 days postpartum had infants with the longest average hospital length of stay than women who were provided any form of prescription contraception. Although the results from Aim 3 were consistent with the results from Aims 1 and 2, there were issues of differential selection bias in the Aim 3 cohort as women with OUD/Bup were less

likely to be linked with an infant record compared to women with non-chronic and chronic prescription opioid use.

4.7 References

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Chapter 5. Discussion

5.1 Overview

This chapter discusses the results of the three research aims examined in this dissertation. The aims were: Aim 1) Evaluate the association between opioid use during pregnancy and prescription contraception provision by 60 days postpartum, including by contraceptive method type; Aim 2) Evaluate the time to first prescription contraception provision during the postpartum period for women who did and did not use opioids during pregnancy, including by type of opioid; and Aim 3) Assess if adverse newborn outcomes are associated with provision of prescription contraception within 60 days postpartum among women who used opioids during pregnancy. This chapter begins with a brief overview of the study methods, a discussion of the main findings from each aim, followed by a discussion of the study strengths and limitations, public health implications, and conclusions of the research.

5.2 Study Overview

Aim 1 evaluated the relationship between opioid use during pregnancy and provision of prescription contraception within 60 days postpartum. The analytic cohort included women with a livebirth between January 2011 and November 2017 who maintained health and pharmaceutical insurance coverage for the duration of pregnancy and for at least the first 60 days postpartum (n=1,291,352). Aim 1 addressed two outcomes: a binary measure of any postpartum prescription contraception within 60 days postpartum and a categorical measure of contraceptive provision by method type, again measured over the first 60 days postpartum. Contraceptive method type included female sterilization, LARC, and moderately effective methods (MEM), with no evidence of prescription contraception provision as the reference category. Bivariate and multivariable logistic regression models were used for the analysis of any postpartum prescription contraception. Multinomial regression models were used for the categorical

measure of contraceptive provision by method type. Covariates included maternal age, several geographic-based variables (HRSA region, state-level characteristics), year of delivery, and select clinical variables including several comorbidities (non-opioid substance use disorders, psychiatric conditions, chronic hypertension, gestational hypertension, diabetes mellitus, gestational diabetes, asthma, autoimmune disease, pain conditions), delivery mode, and postpartum care visit attendance within 60 days postpartum.

Aim 2 evaluated the association between opioid use during pregnancy and time to provision of contraception within the first 365 days postpartum. Women in the Aim 2 analytic cohort had a livebirth between January 2011 and December 2016 and maintained continuous health and pharmaceutical insurance coverage for the duration of pregnancy and for some length of time during the postpartum period (n=1,270,832). Aim 2 relied on survival analysis techniques beginning with several univariate analyses calculating the mean time to contraceptive provision, Kaplan-Meier curves, and Log-Log plots. Bivariate Cox Proportional Hazard models were used to assess the unadjusted relationship between the covariates and postpartum contraceptive provision. Finally, multivariable Cox Proportional Hazards models estimated the adjusted hazard ratio for contraceptive provision up to 365 days postpartum. The multivariable Cox models were adjusted for maternal age, the geographic-based variables, year of delivery, and select clinical variables including several comorbidities and delivery mode.

Aim 3 evaluated if adverse newborn outcomes impacted contraceptive provision within 60 days postpartum among women who used opioids during pregnancy. The newborn outcomes examined were neonatal abstinence syndrome (NAS) diagnosis, neonatal intensive care unit (NICU) admission, and hospital length of stay. The Aim 3 analytic cohort began with the subgroup of women from Aim 1 who used opioids during pregnancy. Women who were

successfully linked with an infant record were included in the sample for the Aim 3 analysis (n=63,897). Bivariate and multivariable logistic regression models were used to evaluate the relationship of type of opioid use during pregnancy and infant outcomes with any prescription contraceptive provision within 60 days postpartum. The multivariable model was adjusted for maternal age, the geographic-based variables, year of delivery, select comorbidities, and other clinical variables.

5.3 Aim 1 Discussion

Aim 1: Evaluate the association between opioid use during pregnancy and prescription contraception provision by 60 days postpartum, including by contraceptive method type.

Opioid use during pregnancy was documented in 9.6% of women in the Aim 1 cohort from 2010-2017, with 88.3% having non-chronic prescription opioid use, 7.5% with chronic prescription opioid use, and 4.1% with an OUD diagnosis or Buprenorphine prescription (OUD/Bup). Over the study period, 37.6% of women were provided some form of prescription contraception within 60 days postpartum. Results showed that women with non-chronic and chronic prescription opioid use during pregnancy had significantly higher odds of prescription contraceptive provision than women who did not use opioids; women with OUD/Bup had significantly lower odds of contraceptive provision. The adjusted odds of contraceptive provision within 60 days postpartum was 1.13 (95% CI: 1.12-1.15) and 1.19 (CI: 1.14-1.24) times higher for women with non-chronic and chronic prescription opioid use compared to women who did not use opioids. Women with OUD/Bup had 20 percent lower odds of receiving postpartum prescription contraception (aOR: 0.80, 95% CI: 0.75-0.85) than women who did not use opioids.

Significant differences in contraceptive provision were also observed by method type. Women in every category of opioid use had a significantly increased adjusted relative risk ratio (aRRR) of sterilization verses no method than women who did not use opioids. The aRRR of sterilization verses no method for women with non-chronic prescription use was 1.49 (95% CI: 1.46-1.53); 2.12 (95% CI: 1.99-2.26) for women with chronic prescription use; and 1.32 (95% CI: 1.16-1.50) for women with OUD/Bup. Women with non-chronic prescription use also had significantly increased aRRR for LARC (aRRR: 1.10, 95% CI: 1.07-1.12) and MEM (aRRR: 1.05, 95% CI: 1.03-1.06) provision verses no method relative to women who did not use opioids. The aRRR for LARC and MEM provision for women with chronic prescription use did not differ significantly compared to women with no opioid use during pregnancy. Women with OUD/Bup had significantly lower aRRR for LARC (aRRR: 0.73, 95% CI:0.65-0.82) and MEM (aRRR: 0.73, 95% CI: 0.68-0.79) provision verses no method compared to women who did not use opioids.

Our study results are comparable to prior literature for women with OUD/Bup, but few studies had included women by other types of opioid use, as defined in our study. The level of opioid use during pregnancy observed in this study was consistent with prior literature examining the privately insured population [1]. Similarly, the results of previous research examining contraception use among women who use opioids, including during pregnancy, has generally noted that women who use opioids have lower or comparable levels of contraception use to that for women who do not use opioids [2-11]. Many studies, however, lack a direct comparison group of women who do not use opioids and generally only included women with OUD or who were currently enrolled in medication-assisted therapy (MAT) programs for OUD treatment. Few studies specifically examined postpartum contraception among women who used

opioids or other substances during pregnancy. The results of a study of pregnant women enrolled in a randomized trial to treat substance use disorders (SUD) showed postpartum contraceptive rates of approximately 70% over the first 24 months postpartum, comparable to postpartum contraceptive levels observed in non-SUD populations [9]. Several other studies reported postpartum contraception levels for women with OUD or other SUDs far below this rate, ranging from 25%-50% [3-5, 11].

Investigators using Tennessee PRAMS data reported that women with substance use during pregnancy had lower levels of postpartum contraception use than women who did not use substances (79.6% vs 88.1%, P=0.019) [7]. A single study examining contraceptive claims among non-pregnant women of reproductive age with chronic prescription opioid use reported that 23.4% of women had any indication of prescription contraception, again lower than the national average of 64.9% [10, 12]. The results of studies among the broader population of women of reproductive age with OUD or other SUDs have consistently indicated that women with SUDs have lower contraceptive prevalence, favor less effective methods such as condoms, and generally have lower use of highly effective methods such as LARC than women without SUDs [2, 6, 8].

The current study involved stratifying by type of opioid use during pregnancy, and the observed findings indicated that both the overall level of use and type of postpartum contraceptive method differed across the three opioid use groups in comparison to women who did not use opioids. Furthermore, the study results demonstrated that women who use opioids during pregnancy are not a homogenous group, but in fact, differ across important variables such as age and prevalence of comorbidities depending on the pattern and type of opioid use. The higher levels of postpartum contraception among women with chronic and non-chronic

prescription use, particularly for sterilization, seem logical. Women prescribed opioids during pregnancy are likely experiencing acute pain or chronic conditions which may complicate their pregnancy and require more frequent contacts with healthcare providers [1, 13-15]. Women with complicated pregnancies have higher rates of postpartum visit attendance which is also associated with higher postpartum contraceptive provision [16, 17]. Furthermore, women in the chronic prescription opioid group were older, on average, compared to the larger Aim 1 cohort; age is directly related to parity and parity is highly predictive of postpartum contraception use [18, 19]. Parity could not be examined in the current study, but taken together, these factors may explain the higher levels of postpartum contraception observed in the non-chronic and chronic prescription opioid use groups.

The lower odds of any prescription contraception provision among women with OUD/Bup is supported by prior literature. However, the observed increase in sterilization and simultaneous lower relative risk ratio of LARC or MEM provision is a new finding. Women with OUD/Bup may have high risk pregnancies resulting in a higher likelihood of sterilization at the time of delivery while also having lower rates of postpartum follow up care within 60 days of delivery, and, accordingly, reduced levels of LARC and MEM provision [20]. Prior literature has documented low levels of postpartum visit attendance in women with OUD, which is common when LARC and MEM are provided to postpartum women [11, 21].

The overall level of opioid use documented in this study was consistent with prior literature examining opioid use during pregnancy among the privately insured population [1]. Bateman et al reported 14.4% of privately insured pregnant women were prescribed at least one opioid during pregnancy, with a prevalence of 12.9% in 2011, similar to the level of opioid exposure observed in this study in 2011, 11.2% [1]. A second study within a large health system

in the Midwest reported 12.3% of pregnancies from 2006-2014 had evidence of opioid use [15]. Like the trends reported in the population at large, opioid use during pregnancy decreased over the study period from a high of 11.2% in 2011 to 4.4% in 2017 [22].

The observed decrease in opioid use over time in the current study, particularly for prescription opioids, is also consistent with larger national trends over a similar time period, which reflect decreased use and prescribing of prescription opioids [22]. Despite declining rates of opioid prescribing in the US, use of illicit opioids such as heroin and illicitly manufactured fentanyl has been increasing since 2007 [23, 24]. Use of illicit forms of opioids is difficult to measure in administrative claims data without an explicit diagnosis of OUD or other substance use disorder, or an overdose event and may result in some exposure misclassification. The level of opioid use during pregnancy observed in this study was lower than levels documented among Medicaid recipients. The results of two studies noted that 21%-29% of pregnant women enrolled in Medicaid were prescribed an opioid at some point during pregnancy; however, these estimates are somewhat dated, ranging from 1995-2009 [13, 25]. OUD/Bup was more common in the Aim 1 cohort among younger women, women with concomitant non-opioid SUDs, and psychiatric illness. Chronic prescription opioid use was more common among older women, and women with chronic conditions such as autoimmune disorders, pain conditions, diabetes, and hypertension.

The levels and method-specific results for postpartum prescription contraception found in this study were consistent with a similar study conducted in 2015, which used the MarketScan database and the NQF postpartum contraception performance measures. The 2015 study examined postpartum contraception among privately insured women from 2005-2014 [26]. Law et al reported age stratified results but the levels of provision for woman aged 21-44 were similar

to those in the overall Aim 1 cohort for the overlapping years (2011-2014). The study authors also reported increased LARC provision during their study period and decreasing levels of sterilization, both of which were observed in the current study.

Postpartum prescription contraceptive provision also was significantly associated with several demographic characteristics including maternal age, HRSA region, state-level characteristics, and year of delivery in the Aim 1 cohort. Several studies have documented decreased odds of postpartum contraceptive provision as age increases, a trend observed in this research [18, 27, 28]. Although increasing age was associated with decreased odds of any contraceptive provision, the aRRR for sterilization increased with age; conversely, the aRRR for LARC provision was highest for younger women (<25 years). The aRRR for MEM provision was significantly lower for every age group relative to the reference group, women aged 25-29. The method-specific age patterns observed in this study are consistent with prior literature [18, 19, 29, 30].

Regional differences in postpartum contraception are well-documented in the literature with higher levels in the Southern US, driven by high levels of sterilization and MEM provision [18, 29-32]. In this study, HRSA Region 6 (TX, LA, AR, OK, NM), had the highest aRRR for sterilization and MEM provision; Region 8 (Western Region) had the highest aRRR for LARC provision. Year of delivery was associated with a gradual decrease in the odds of any postpartum contraceptive provision; based on the method-specific models, this decrease was largely driven by a decline in sterilization over the study time period, a trend observed in national-level data [12, 30]. LARC provision increased over the study period, with the highest aRRR observed in 2017, again consistent with broader trends indicating increased postpartum LARC use in the US [12, 30, 33].

Consistent with results from other studies, mode of delivery and attending a postpartum care visit within 60 days of delivery were both positively associated with provision of contraception. Cesarean deliveries were associated with higher odds of postpartum contraceptive provision, particularly sterilization. Prior literature has shown cesarean delivery to be a strong predictor of completed female sterilization [30, 34-36]. Results of prior studies have also documented a strong relationship between a postpartum care visit and postpartum contraception, with a pronounced relationship between postpartum care visits and use of highly effective contraception, including LARCs as observed in the current study [16, 18, 37].

Psychiatric disorders, chronic hypertension, and asthma were associated with increased contraceptive provision; gestational hypertension, gestational diabetes, and autoimmune disease were associated with decreased provision of any postpartum prescription contraception. The relative risk for sterilization was significantly increased for women with every comorbidity, except gestational hypertension and autoimmune disease. LARC provision was not as strongly associated with maternal comorbidities. Psychiatric disorders, chronic hypertension, and asthma significantly increased the relative risk ratio of LARC provision whereas gestational diabetes significantly decreased the relative risk ratio verses no provision. Chronic hypertension, gestational hypertension, and asthma were associated with an increased relative risk of MEM provision verses no provision compared to women without these conditions. Non-opioid SUD, diabetes, both pre-existing and gestational, as well as pain conditions were associated with a decreased relative risk of MEM provision verses no provision compared to women without these conditions.

There is limited research examining how experiencing a medically complex pregnancy influences postpartum contraceptive provision or use. The results of a 2015 study suggested that

women with high-risk pregnancies had slightly higher interest in highly effective contraception at the time of hospital discharge and at the postpartum visit, but similar rates of provision compared to women with low-risk pregnancies [38]. In a second study examining immediate postpartum LARC and sterilization, maternal medical comorbidities were significantly associated with both immediate LARC and sterilization, with a stronger relationship for immediate LARC provision [30]. Women who experience a medically complex or high-risk pregnancy may be motivated to avoid unintended pregnancy and thus be inclined to choose highly effective methods such as sterilization or LARC. Future research is needed to clarify the relationship between experiencing a medically complex pregnancy and postpartum maternal care-seeking behavior, including provision of postpartum contraception.

The finding that chronic and gestational hypertension were associated with a significantly increased aRRR for MEM provision relative to no provision compared to women without hypertension was unexpected. The US Medical Eligibility Criteria for Contraceptive Use rates combined hormonal contraceptives (CHC) as a "3" and "4" for women with hypertension, indicating that the risks associated with CHC use in women with hypertension outweigh the advantages [39]. Although there are progestin-only and non-hormonal methods of contraception included in the definition for MEM, the combined hormonal pill is among the most popular forms of contraception in the US and it is likely that a significant proportion of MEM users in this population are using a combined hormonal pill [40]. Future research is needed to examine the use of postpartum CHCs in women with hypertension as it may increase the risk of stroke, myocardial infarction, and venous thromboembolism [41-48]. The decreased aRRR of provision of MEM for women with pain conditions may be due to the inclusion of headaches in the definition of pain conditions. Women who experience migraines with aura are at significantly

increased risk for ischemic stroke and the use of CHCs further increases this risk; therefore, CHCs are not recommended for women with this condition [39, 49-52].

5.4 Aim 2 Discussion

Aim 2: Evaluate the time to first prescription contraception provision during the postpartum period for women who did and did not use opioids during pregnancy, including by type of opioid.

The Aim 2 analysis examined postpartum prescription contraception provision over the first 365 days postpartum using survival analysis. The prevalence of opioid use during pregnancy was comparable to levels observed in Aim 1: overall, 10.1% of women had any evidence of opioid use. Among women with evidence of opioid use, 88.3% had non-chronic prescription use; 7.7% had chronic prescription use; and 4.0% had OUD/Bup. Within 365 days of delivery, 50.2% of women were provided some form of prescription contraception, with 31.7% receiving MEM, 11.9% receiving LARC, and 6.6% undergoing sterilization. In the fully adjusted Cox models, women with non-chronic and chronic prescription opioid use were more likely to receive contraception, whereas women with OUD/Bup were significantly less likely to receive any prescription contraception. The adjusted-average time to contraceptive provision among women who received contraception within 365 days postpartum was significantly different for women in all categories of opioid use compared to women who did not use opioids. Women with OUD/Bup had the longest average time to contraceptive provision while women with chronic prescription use had the shortest average time to provision among the opioid use groups, including women who did not use opioids during pregnancy.

Women with non-chronic prescription opioid use had an adjusted hazard of contraceptive provision 1.15 (95% CI: 1.14-1.16) times higher than women who did not use opioids during pregnancy. The adjusted hazard for women with chronic prescription opioid use

was even higher at 1.24 (95% CI: 1.21-1.27) compared to women who did not use opioids. Women with OUD/Bup had a significantly lower hazard of 0.93 (95% CI: 0.89-0.97) compared to women who did not use opioids. These results reflect the larger overall pattern in this study of higher postpartum contraceptive provision among women with non-chronic and chronic prescription opioid use and lower provision for women with OUD/Bup compared to women who did not use opioids. The pattern of contraceptive provision in the OUD/Bup group changed over the postpartum period. In the first 60 days postpartum, women with OUD/Bup had a significantly lower hazard of contraceptive provision (aHR: 0.85, 95% CI: 0.81-0.90), but from 61-365 days postpartum, the hazard of contraceptive provision for women with OUD/Bup did not differ significantly from that for women who did not use opioids (aHR: 1.05, 95% CI: 0.99-1.13). This finding suggests that women with OUD/Bup may be less likely to receive postpartum contraception in the first 60 days following delivery but after that time, the disparity in contraceptive provision attenuates for women with OUD/Bup compared to women who did not use opioids and did not receive contraception within 60 days postpartum.

There are several possible reasons for the changing hazard over time for women with OUD/Bup based on prior literature and findings from the current study. Foremost, women with OUD/Bup have low rates of postpartum visit attendance [4, 11, 21]. Women with OUD/Bup may eventually attend a postpartum visit but after the recommended 60 days following delivery. Secondly, women identified as having OUD during pregnancy, even those currently in treatment, are often subject to increased stigma and scrutiny, which may make them less likely to return for a postpartum visit [53-55]. Finally, their infants may be at high risk for complications and if their infant is hospitalized for a prolonged period of time, it may delay postpartum care-seeking for the mother [20, 28, 56-59]. This hypothesis is supported by the results from Aim 3, showing

that among women who use opioids during pregnancy, increased infant hospital length of stay significantly reduced the odds of postpartum contraceptive provision. Infants born to women with OUD/Bup had the longest average hospital length of stay of the three opioid-use groups. The hazard of contraceptive provision for women with non-chronic and chronic prescription opioid use compared to women who did not use opioids was consistent across all time periods. To our knowledge, this study is the first to examine time to contraceptive provision over the first 365 days postpartum by type of opioid use during pregnancy.

The adjusted mean days to postpartum contraceptive provision was calculated for women who received prescription contraception at any point during the first 365 days postpartum. The analysis was adjusted for maternal age, the geographic variables, year of delivery, and select clinical variables including several comorbidities and delivery mode. In the adjusted analysis, women with OUD/Bup had the longest average time to contraceptive provision at 72.32 days (95% CI: 69.99-74.64) while women with chronic prescription use had the shortest time at 54.88 days (95% CI: 53.28-56.47). Women with non-chronic use had an average time to contraceptive provision of 59.34 days (95% CI: 58.86-59.81) and women with no opioid use received contraception, on average, at 61.92 days postpartum (95% CI: 61.76-62.08). The longer average time to contraceptive provision among women with OUD/Bup helps explain the earlier finding of shifting hazards of contraceptive provision over the postpartum period. Many women with OUD/Bup who ultimately used contraception received it after the recommended time period for a postpartum care visit.

The overall pattern of time to contraceptive provision in the first year postpartum observed in this study is similar to that reported in a 2018 study examining postpartum contraceptive use by birth intendedness [60]. The study authors observed a sharp increase in

contraceptive uptake in the first three months postpartum, a slower increase in uptake in months three through six, and a plateauing there after [60].

In general, the adjusted hazard ratio of contraceptive provision for the covariates was consistent with the overall associations observed in Aim 1. The hazard for contraceptive provision for maternal age and delivery mode, however, exhibited changes over the postpartum period that require further explanation. Women in the two youngest age groups, <20 and 20-24 years, had a slight but significantly decreased hazard of contraceptive provision in the first 60 days postpartum. In the 61-365 days postpartum period, women in these age groups had a significantly increased hazard of contraceptive provision compared to women age 25-29 who had not received prescription contraception in the first 60 days postpartum. This pattern is likely due to the higher prevalence of LARC provision in the youngest age groups, which is also the method type with the longest average time to provision at 76.58 days following delivery (95% CI: 76.30-76.86) [19].

A similar, but inverse, relationship was observed for women with cesarean deliveries: in the first 60 days postpartum, women with cesarean deliveries had a significantly higher hazard of contraceptive provision (aHR: 1.43, 95% CI: 1.42-1.44) than women with vaginal births. In the 61-365 days postpartum, there was no significant difference in the hazard of contraceptive provision for women with a cesarean delivery compared to those with a vaginal delivery. This relationship is likely due to the high prevalence of sterilization in women with cesarean deliveries [30, 35, 36]. The shortest average time to provision of any method following delivery was sterilization at 13.26 days (95% CI: 12.98-13.54).

5.5 Aim 3 Discussion

Aim 3: Assess if adverse newborn outcomes are associated with provision of prescription contraception within 60 days postpartum among women who used opioids during pregnancy.

The Aim 3 analysis was restricted to women with evidence of opioid use during pregnancy for whom infant data were linked; 89.8% of women had evidence of non-chronic prescription use during pregnancy; 7.6% of women had chronic prescription opioid use; and 2.5% OUD/Bup use. Over the study period, 41.6% of these women were provided some form of prescription contraception within 60 days postpartum. The study results showed that among women who used opioids during pregnancy, each one-day increase in infant hospital length of stay (LOS) resulted in a 1.1% decrease in the odds of receiving postpartum prescription contraception within 60 days of delivery (aOR: 0.989, 95% CI: 0.986-0.991). NAS diagnosis and NICU admission for the infant were not significantly associated with provision of postpartum contraception in the fully adjusted analysis.

In unadjusted analyses, the mean hospital LOS varied significantly by contraceptive provision and method type. Newborns of women not provided contraception within 60 days postpartum had an average hospital LOS of 4.8 days (95% CI: 4.74-9.93) whereas the average hospital LOS for newborns of women provided contraception was 4.2 days (95% CI: 4.13-4.32). The shortest average LOS was noted for women ultimately provided LARC (mean days: 3.8, 95% CI: 3.60-4.04).

The significant decrease in postpartum contraceptive provision with each one-day increase in infant hospital LOS in the fully adjusted model suggests a relationship between severity of illness in the newborn and postpartum contraception use. Few studies have examined the relationship between infant hospital LOS and postpartum contraception use; rather studies

have focused on specific adverse outcomes in the infant such as preterm birth or low birth weight. Prior studies show lower levels of postpartum contraception use among women with preterm infants and medically complicated pregnancies [28, 61] with a general trend towards the prioritization of infant well-being [56-58, 62]. A 2019 qualitative study found that women with preterm infants in the NICU prioritized decision-making related to infant well-being and questioned the timing of immediate postpartum contraceptive counseling because of existing stress associated with having a traumatic birth experience and hospitalized infant [56]. A second qualitative study noted that women with infants still-hospitalized six weeks after delivery were reluctant or unable to attend a postpartum care visit because they did not want to leave the hospital and felt emotionally unable to focus on their own care [62]. In the current study, longer hospital LOS for infants born to women with evidence of opioid use during pregnancy resulted in lower postpartum contraceptive provision, in keeping with previous findings but adding information to our understanding of how adverse infant outcomes impact maternal postpartum care. Future studies will need to expand the study population to include women without opioid use and explore the mechanisms underlying lower postpartum contraception use among women with severely ill infants more generally.

Approximately 13% of newborns in the Aim 3 cohort were admitted to the NICU, higher than the national average of 7.8% of all livebirths [63]. This finding was expected for two reasons. First, the Aim 3 analysis was restricted to women with evidence of opioid use during pregnancy, increasing the likelihood of a medically complex pregnancy with consequences in the infant [20]. Secondly, the successful linkage between women and their infants may be biased towards certain groups of women with infants who are more likely to be admitted to the NICU. Women from the OUD/Bup group were underrepresented in the final Aim 3 cohort because a

lower percentage of women from this group were successfully linked with their newborns. Over 50% of women in the non-chronic and chronic prescription opioid use groups were successfully linked, whereas just 31.6% of women from the OUD/Bup group were linked with their newborn. The reason why the linkage rate for women in the OUD/Bup group was substantially lower is unknown, but an important area for future research. In the unadjusted analysis, NICU admission was associated with lower odds of contraceptive provision but after adjustment, this association was no longer significant, likely due to its relation to longer infant hospital length of stay.

The percentage of infants diagnosed with NAS in the Aim 3 cohort increased over the study period from 0.9% in 2011 to 3.5% in 2017, consistent with national trends indicating an increase in NAS and neonatal opioid withdrawal syndrome (NOWS) diagnoses [64]. The proportion of newborns with NAS was substantially higher in the Aim 3 cohort than levels observed in national data, as expected because the Aim 3 cohort was restricted to women with evidence of opioid use during pregnancy [64]. In 2014, 0.2% of hospital births paid for by private insurance had an NAS or NOWS diagnosis, where-as 1.7% of the infants born in 2014 in the Aim 3 cohort were diagnosed with NAS [64]. Like the findings for NICU admission, NAS was associated with lower odds of contraceptive provision in the unadjusted analysis but was no longer significant in the fully adjusted analysis.

The association between contraceptive provision and type of opioid use during pregnancy was consistent with the relationship observed in Aim 1. Women with chronic prescription opioid use during pregnancy had significantly higher odds of prescription contraceptive provision while women with OUD/Bup had significantly lower odds compared to women with non-chronic prescription opioid use. The adjusted odds of contraceptive provision within 60 days postpartum was 1.11 (95% CI: 1.05-1.18) times higher for women chronic prescription opioid and 17%

lower for women with OUD/Bup (aOR: 0.83, 95% CI: 0.72-0.94) than women with non-chronic prescription opioid use. The association between the other covariables and provision of contraception were similar to those observed in Aim 1 and largely supported by prior literature.

5.6 Study Strengths

This research has several strengths. To our knowledge, this study is the first to examine postpartum contraceptive provision among privately insured patients in the US, comparing women who used opioids during pregnancy with those who did not. The inclusion of a comparison group of women who did not use opioids during pregnancy is a significant strength as few studies with similar research aims included a comparison group. While the study of Medicaid patients and women without health insurance remains important, privately insured patients are a significant population of interest, representing 46% of births annually in the US [65].

The sample size afforded by MarketScan provided this study with ample power to detect meaningful differences between different groups of opioid users, the first study to do so. This study strength is particularly important as significant differences in contraceptive provision were found for each group as well as distinct demographic and clinical profiles. Although the MarketScan database is a convenience sample of individuals with employer-based health insurance plans, the large number of individuals captured on an annual basis helps increase the external validity of this research. For example, in 2018, the MarketScan database contained data for more than 41.2 million individuals, a large enough cohort to create a nationwide sample of patients with employer-based insurance in the US [66]. The large number of observations in this research lent stability to the survival analysis and hazard estimates, which can often be unreliable as the number of observations decreases with increasing length of follow-up.

Prior to making the MarketScan data public, the data undergoes numerous quality checks and has limited missingness. The unique enrollment and family identification codes assigned to individuals in the MarketScan database allow for follow up of individuals over time. The current study leveraged the longitudinal nature the data and included variables from the prenatal, perinatal, and postnatal time periods as well as using multiple time points to measure contraceptive provision. The study employed evidence-based performance quality measures for postpartum contraception [67]. These measures have been used in prior studies and increase both the interpretability and applicability of the study results [26, 67]. Finally, because the dataset captured all inpatient, outpatient, and outpatient prescriptions claims for a woman over the enrollment period, it included critical variables that may not be accessible when using sources such as electronic medical records or national survey data.

5.7 Study Limitations

This research also has limitations. Foremost, the MarketScan database only contains claims for privately insured patients, a limitation for several reasons. First, while close to half of births in the US were covered by private insurance in 2017, just over 40% were insured by Medicaid; therefore, these births are not captured by the MarketScan database [68]. Secondly, prior research indicates that rates of opioid prescribing, opioid misuse, and OUD are higher in Medicaid populations than the general and privately insured populations [13, 69, 70]. Finally, the use of MarketScan data limits the generalizability of these results to privately insured patients with employer-provided insurance, who are more likely to be White, have higher incomes, and higher education [71]. While this is a major limitation of the current study, two-thirds of Americans are covered through private health insurance plans and there are currently no studies that have examined these research aims in a privately insured population [71]. Although the data

source limits the generalizability of the results, the privately insured population is under-studied and this research addresses a gap in the existing literature.

A second limitation of this research is the lack of available data about non-prescription contraceptive methods such as male condoms and sterilization procedures among male partners. Prior research indicates that condoms are the preferred method among women with OUD, thus the exclusion of non-prescription contraceptive methods may result in an underestimation of postpartum contraception use [2]. The findings can only be interpreted to use of moderately and highly effective prescription methods, an important consideration nevertheless regarding pregnancy prevention.

There also were limitations identifying the full spectrum of opioid use during pregnancy. Due to regulations surrounding the administration of methadone as treatment for OUD, methadone was not captured in private insurance claims data. This limitation likely resulted in missed cases of women with OUD. However, both buprenorphine and naltrexone, the other two FDA approved medications for treating OUD, are not subject to the same restrictions and were captured in the MarketScan database. Prior research indicates that among people on MAT, use of buprenorphine is increasing particularly since 2009, which may help decrease the degree of exposure misclassification in this study if fewer patients are being treated with methadone in favor of buprenorphine [72].

The MarketScan database also lacks important sociodemographic variables such as race/ethnicity, parity, education, and marital status which are strongly associated with postpartum contraceptive use [73]. Efforts were made to attenuate the impact of these missing sociodemographic variables by incorporating state-level characteristics such as racial composition, poverty level, and educational attainment. There was also concern over differential

loss to follow up because women with the most severe addiction or those with serious comorbidities may be less likely to have continuous insurance enrollment or may qualify for public forms of insurance. The continuous enrollment inclusion criterion for each Aim were designed to minimize the potential impact of this bias. A sensitivity analysis was performed for each research Aim comparing women who met the inclusion criteria with those who did not; except for Aim 3, no major differences emerged.

A limitation of the Aim 3 analysis is the relatively low percentage of women who were successfully linked with an infant record (51.5%), which may bias the results as women in the OUD/Bup group were underrepresented in the final Aim 3 cohort. A sensitivity analysis indicated selection bias in the Aim 3 cohort resulting in an overestimate of the association between OUD/Bup and postpartum contraceptive provision. The linkage rates of maternal-infant records reported in prior studies using administrative claims data vary widely from 45%-90% and fluctuate depending on data source, inclusion criteria, direction of linkage, and exposure of interest [74]. Several studies using the MarketScan database have linked maternal-infant records with linkage rates varying from 50%-75% [75-77]. The study with the highest linkage rate used the commercial and Medicaid components of the Marketscan database; the authors also reported the linkage rate as the percentage of liveborn infants linked to a maternal record which tends to yield higher rates than reporting the percent of maternal records linked with a liveborn infant [77].

5.8 Public Health Implications

Overall, this research contributes to our limited understanding of postpartum contraceptive patterns among women who use opioids during pregnancy, providing special insight into differences by type and pattern of opioid use among privately insured women. Our

study findings consistently indicated that women with OUD/Bup were less likely to receive prescription contraception in the postpartum period than women who did not use opioids. Furthermore, the study findings indicate that women with non-chronic and chronic prescription opioid use during pregnancy are more likely to be provided postpartum contraception than women who do not use opioids, a new finding. This finding highlights the need to differentiate between opioid-use type when developing clinical guidelines and policies that address maternal health needs. The public health implications of this research include tailoring antenatal and postpartum care for women with various types of opioid use, decreasing barriers to immediate postpartum LARC especially among the privately insured population, and considering and incorporating the health status of the infant into clinical guidance for postpartum maternal healthcare.

This research highlighted stark demographic and clinical differences between women with OUD/Bup, non-chronic and chronic prescription opioid use during pregnancy. These results, disaggregated by type of opioid use during pregnancy, offer an opportunity for clinicians and public health professionals to develop tailored clinical guidance for how best to care for these women in the antenatal and postpartum period. It is imperative that contraceptive counseling guidelines are non-coercive and collaborative, particularly in the context of a drug-using population as there is a history of targeting these populations for long-acting or permanent forms of contraception using coercive incentives and counseling [78, 79]. A 2019 review by Heil et al described several quasi-experimental studies examining the efficacy of co-locating drug treatment and family planning services on contraceptive uptake [5, 80-83]. These integrated care models appear to hold promise for promoting contraceptive use among women with OUD/Bup in a convenient, safe, and non-judgmental atmosphere.

The results of two quasi-experimental studies showed significant increases in contraceptive uptake for women receiving interventions designed specifically for OUD populations. In a 2016 study, women with OUD in the intervention group were provided with the contraceptive method of their choice free-of-charge with immediate on-site initiation plus an additional six months of follow-up visits to manage side effects and contraceptive adherence [80]. Women in the intervention group universally initiated contraception compared with 29% of women in the usual care group; contraceptive continuation was also higher in the intervention group over the six-month follow-up period [80]. Findings of a second study, focused on postpartum contraception, indicated that using women-centered OUD treatment services during pregnancy resulted in higher postpartum visit attendance and postpartum LARC use compared to women provided usual OUD treatment [81].

An integrated program from 2005-2009 provided contraceptive services to women in a pediatric clinic located within a drug treatment facility [83]. Women participated in ante- and postpartum group education sessions focused on contraception and were able to receive the method of their choice free-of-charge. Although no comparison group was included, 70% of women requested postpartum contraception and 68% ultimately received a method [83]. In a retrospective chart review, Collier et al did not find significant differences in interpregnancy interval or contraceptive uptake between women receiving medication assisted therapy (MAT) co-located at an obstetric office compared to those receiving MAT at a community MAT program [5]. The authors note, however, that co-location of MAT and obstetric services was not available in the immediate postpartum period which likely influenced contraceptive uptake. These programs and interventions provide an encouraging avenue for ensuring that pregnant women with OUD/Bup can make informed decisions about postpartum contraception and

conveniently access their method of choice. Our research findings demonstrate that more interventions are needed to address the disparity in postpartum contraceptive provision for women with OUD/Bup.

Immediate postpartum LARC insertion, defined as LARC insertion prior to hospital discharge following delivery, is safe and acceptable among women of reproductive age; yet the rates of immediate LARC insertion remain low, especially among privately insured women [30, 84, 85]. In the current study, immediate postpartum LARC provision was very low, with approximately 0.1% of women receiving immediate postpartum LARC, consistent with levels observed in other studies of privately insured women [26]. Immediate postpartum LARC increases optimal birth spacing, decreases unintended and mistimed pregnancies, and is highly cost-effective [84, 86, 87]. Decreasing barriers to postpartum LARC not only benefit the broader population of postpartum women, but also may help address the disparity in contraceptive provision and timing observed in the current study for women with OUD/Bup.

In a 2017 study among a nationally representative sample of postpartum women, women with non-private insurance were significantly more likely to receive immediate postpartum LARC than women with private insurance [30]. The differential rates of immediate postpartum LARC use by insurance type are likely due to differences in reimbursement practices. Starting in 2012, several state Medicaid programs began reimbursing for the LARC device and insertion procedure during the hospital stay for delivery, separately from the bundled labor and delivery reimbursement fee [88]. Currently, 37 state Medicaid programs reimburse for immediate postpartum LARC insertion [89]. Conversely, very few private insurance companies have moved to reimburse for the LARC device or insertion procedure during the hospital stay for delivery, although both are universally covered in an outpatient setting.

Expanding access to immediate postpartum LARCs through changes to insurance reimbursement may help decrease disparities in postpartum contraception for several reasons. It is estimated that up to 40% of women do not receive a postpartum visit, and these rates are even higher among the OUD/Bup population, making immediate insertion a convenient and safe option for women who choose to use these methods [4, 11, 16, 90]. Among women who intend to use LARCs postpartum, studies show that 40%-75% do not end up receiving their method of choice [91, 92]. Removing financial and logistical barriers to immediate postpartum LARC insertion will help ensure that even when women do not attend a postpartum visit, they have an opportunity to obtain LARC if they choose to do so. Up to 80% of pregnancies to women with OUD are unintended and in conjunction with low postpartum visit attendance, increasing access to immediate postpartum LARC insertion can help close gaps in contraceptive provision and prevent unintended and mistimed pregnancies for all postpartum women [93, 94].

There is limited research on how the health status of an infant impacts the postpartum healthcare seeking behavior of the mother. The current research found an association between infant hospital length of stay and postpartum contraceptive provision among women who used opioids during pregnancy, suggesting that women with severely ill infants have lower levels of contraceptive provision. This area is ripe for future research and potential public health interventions. Counseling strategies that encourage uptake of maternal postpartum care services, while remaining sensitive to the emotional and psychological needs of mothers and parents with severely ill infants, need to be developed. The results of qualitative and quantitative studies demonstrate that women with infants admitted to the NICU are at increased risk for delayed or inadequate postpartum care given their concern with their infant's health [56, 59, 95].

Crude estimates from a 2016 study indicated that women with preterm, low birth weight infants had a significantly lower postpartum visit attendance compared to women delivering term, normal weight infants [16]. There also is some evidence that interventions designed specifically for women with severely ill infants may increase postpartum care utilization. For example, the results of a quasi-experimental trial among mothers with infants admitted to the NICU showed that an intensive counseling intervention significantly increased postpartum visit attendance among the intervention group compared to the control group [96]. Future research should focus on developing guidelines, counseling techniques, and interventions that improve uptake of postpartum healthcare services among women with critically ill infants.

5.9 Conclusions

This study addressed a gap in the research and added to the literature on postpartum contraception and substance use. Women with non-chronic and chronic prescription opioid use during pregnancy were consistently more likely to receive postpartum prescription contraception at 60 and 365 days postpartum than women who did not use opioids. On the other hand, women with OUD/Bup were significantly less likely to receive contraception, although use showed important nuances over the postpartum period. Women with OUD/Bup were less likely to receive contraception within the first 60 days postpartum but after the 60-day mark, their likelihood of receiving contraception was like that of women who did not use opioids and had also not received contraception within 60 days postpartum. The study findings highlight the need to develop tailored approaches to holistically caring for women during pregnancy and the postpartum period who use opioids, depending on the specific manifestation and reasons for opioid use. Our study also found a strong relationship between hospital length of stay for the infant and postpartum contraceptive provision among women who use opioids during pregnancy.

This finding warrants additional research in an expanded population to better understand the relationship between infant illness and postpartum health care for women overall and those who use opioids and other substances specifically.

5.10 References

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Appendix A

Diagnostic, Procedure, and Drug Codes for All Variables Except National Drug Codes for Prescription Opioids

Table 1. Live Births [1]

Description	Code Type	Codes
Level I		
Outcome of Delivery	ICD-9-CM ICD-10-CM	V27 Z370
Level II		
Normal Delivery	ICD-9-CM ICD-10-CM	650 O80
Level III		
Complicated Cesarean Section	DRG	765
Uncomplicated Cesarean Section	DRG	766
Complicated Vaginal Delivery	DRG	774
Uncomplicated Vaginal Delivery	DRG	775
Uncomplicated vaginal delivery with sterilization and/or dilatation & curettage	DRG	767
Vaginal delivery with operation room procedure except sterilization and/or dilatation & curettage	DRG	768
Level IV: Selected Delivery-Related Procedures		
Forceps	ICD-9-PCS ICD-10-PCS	720, 721, 7221, 7229, 7231, 7239, 724, 726 10D07Z3, 0W8NXZZ, 10D07Z4, 10D07Z5, 10S07ZZ
Breech Extraction	ICD-9-PCS ICD-10-PCS	7251, 7252, 7253, 7254 10D07Z3, 10D07Z4, 10D07Z5, 10D07Z6
Vacuum Extraction	ICD-9-PCS ICD-10-PCS	7271, 7279 0W8NXZZ, 10D07Z6
Other specified and unspecified delivery	ICD-9-PCS ICD-10-PCS	728, 729 10D07Z8
Internal and combined version and extraction	ICD-9-PCS ICD-10-PCS	7322 10D07Z7
Other manually assisted deliveries	ICD-9-PCS ICD-10-PCS	7359 10E0XZZ
Episiotomy	ICD-9-PCS ICD-10-PCS	736 0W8NXZZ
Cesarean Section	ICD-9-PCS ICD-10-PCS	740, 741, 742, 744, 7499 10D00Z0, 10D00Z1, 10D00Z2
Exclusionary Diagnosis and Procedure Codes		
Hydatidiform Mole	ICD-9-CM	630

Description	Code Type	Codes
	ICD-10-CM	O01*, O08*
Abnormal Products of Conception	ICD-9-CM ICD-10-CM	631 O02*, O07* O08*
Ectopic Pregnancy	ICD-9-CM ICD-10-CM	633 O00*, O03*, O08*
Abortion	ICD-9-CM ICD-10-CM	632, 634, 635, 636, 637, 638, 639, 6901, 6951, 7491, 750 Z332, O04*, O07*, 10A07ZZ, 10A08ZZ, 10A00ZZ, 10A03ZZ, 10A04ZZ, 10A07ZX
Stillbirths	ICD-9-CM ICD-10-CM	V271, V274, V277 Z371, Z374, Z377

Table 2. Postpartum Contraception [2]

Contraceptive Method	Codes	Data Source
Female Sterilization	ICD-9: V25.2, V26.51, 662.1, 662.2, 662.9, 663.2	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.2, Z98.51, 0UL.74ZZ, 0UL.78ZZ, 0U5.74ZZ, 0U5.78ZZ, 0UL.74DZ, 0UL.78DZ, 0UL.74CZ, 0UL.70ZZ, 0UL.73ZZ 0UL.77ZZ, 0UL.70CZ, 0UL.70DZ, 0UL.73CZ, 0UL.73DZ, 0UL.77DZ, 0UL.78DZ	
	CPT: 58600, 58605, 58615, 58611, 58670, 58671, 58565	
	HCPCS: A4264	
IUD	ICD-9: V25.11, V25.13, V25.42, V45.51, 996.32, 697	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.430, Z30.433, Z30.431, Z97.5, T83.39XA, 0UH.97HZ, 0UH.98HZ, 0UH.C7HZ, 0UH.C8HZ	
	CPT: 58300	
	HCPCS: J7300, J7301, J7302, S4989, Q0090, S4981	
	NDC: 50419042101, 50419042201, 5128520401	Outpatient Pharmaceutical Claims
Hormonal Implant	ICD-9: V25.5, V25.43, V45.52	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.49, Z30.18	
	CPT: 11981, 11983	
	HCPCS: J7306, J7307	
	NDC: 00052027201, 00052027401, 00052433001	Outpatient Pharmaceutical Claims
DMPA Injection	HCPCS: J1050, J1055	Outpatient Services Claims

Contraceptive Method	Codes	Data Source
		Inpatient Admissions Claims
	NDC: 54569370100, 54569490400, 54569552700, 54569561600, 54569621900, 54868361300, 54868410000, 54868410001, 54868525700, 55045350501, 59762453701, 59762453702, 59762453801, 59762453802, 59762453809	Outpatient Pharmaceutical Claims
Pills	ICD-9: V25.01, V25.41	Outpatient Services Claims Inpatient Admissions Claims
	ICD-10: Z30.011, Z30.41	
	HCPCS: S4993	
	NDC: 00008111720, 00008111730, 00008251402, 00008253505, 00008253601, 00008253605, 00052026106, 00052028306, 00062125100, 00062125115, 00062125120, 00062133220, 00062141116, 00062141123, 00062171400, 00062171415, 00062176100, 00062176115, 00062178100, 00062178115, 00062179600, 00062179615, 00062190120, 00062190320, 000190700, 00062190715, 00062191000, 00062191015, 00247052028, 00247069028, 00247069128, 00247069228, 00247139828, 00247151328, 00247151628, 00247151728, 00247176404, 00247176421, 00247176521, 00247198621, 00247198628, 00247200828, 00247201004, 00247201008, 00247201028, 00247201228, 00247201328, 00247214728, 00247216928, 00247217028, 00247223028, 00247223528, 00247226028, 00247226828, 00378655053, 00378727253, 00378729253, 00430042014, 00430048214, 00430053014, 00430053550, 00430057014, 00430057045, 00430058014, 00430058045, 00430058114, 00430058514, 00430058545, 00555034458, 00555071558, 00555900867, 00555900942, 00555901058, 00555901258, 00555901467, 00555901658, 00555901858, 00555902058, 00555902542, 00555902557, 00555902658, 00555902742, 00555902757, 00555902858, 00555903270, 00555903458, 00555904358, 00555904558, 00555904758, 00555904958, 00555905058, 00555905158, 00555905167, 00555906458, 00555906467, 00555906558, 00555906658, 00555906667, 00555912366, 00555913167, 00555913179, 00603359017, 00603359049, 00603752117, 00603752149, 00603752517, 00603752549, 00603754017, 00603754049, 00603760615, 00603760648, 00603760715, 00603760748, 00603760817, 00603760917, 00603762517, 00603762549, 00603763417, 00603763449, 00603764017, 00603764217, 00603766317, 00603766517, 23490765301, 23490767001, 23490769901, 24090080184,	Outpatient Pharmaceutical Claims

Contraceptive Method	Codes	Data Source
	24090096184, 35356001468, 35356001568, 35356002168, 35356025528, 35356037028, 43386062030, 45802084054, 50419040201, 50419040203, 50419040303, 50419040503, 50419040701, 50419040703, 50419041112, 50419041128, 50419043306, 50419043312, 50452025115, 50458017115, 50458017615, 50458017815, 50458019115, 50458019411, 50458019416, 50458019615, 50458019715, 50458025115, 51285005866, 51285007997, 51285008070, 51285008198, 51285008297, 51285008370, 51285008498, 51285008787, 51285009158, 51285009287, 51285011458, 51285043165, 51285054628, 51285076993, 51285094288, 51285094388, 52544014331, 52544017572, 52544020431, 52544021028, 52544021928, 52544022829, 52544023528, 52544023531, 52544024531, 52544024728, 52544024828, 52544025428, 52544025928, 52544025988, 52544026528, 52544026531, 52544026829, 52544026884, 52544027428, 52544027431, 52544027536, 52544027928, 52544028754, 52544029128, 52544029231, 52544029241, 52544029528, 52544038328, 52544038428, 52544047536, 52544055028, 52544055228, 52544055428, 52544062928, 52544063028, 52544063128, 52544084728, 52544084828, 52544089228, 52544093628, 52544094028, 52544094928, 52544095021, 52544095121, 52544095328, 52544095428, 52544095931, 52544096691, 52544096728, 52544098131, 52544098231, 52959045002, 54569067900, 54569068500, 54569068501, 54569068900, 54569068901, 54569143900, 54569384400, 54569422200, 54569422201, 54569426900, 54569427301, 54569481700, 54569487800, 54569487801, 54569489000, 54569498400, 54569499700, 54569499800, 54569516100, 54569534300, 54569534900, 54569549300, 54569549302, 54569579600, 54569579700, 54569579800, 54569581600, 54569582600, 54569603200, 54569612800, 54569614400, 54569614500, 54569627200, 54569628000, 54569628100, 54868042800, 54868044300, 54868050200, 54868050700, 54868050801, 54868050901, 54868051600, 54868151200, 54868156400, 54868231600, 54868260600, 54868270100, 54868377200, 54868386300, 54868394800, 54868409300, 54868423900, 54868436900, 54868453800, 54868459000, 54868460700, 54868473000, 54868473100, 54868474200, 54868474500, 54868475400, 54868477600, 54868481400, 54868482800, 54868485100, 54868486000, 54868491100, 54868502800, 54868528600, 54868532600, 54868535600, 54868582600, 54868582800, 54868594200, 55045283902, 55045348506, 55045349701, 55045349801, 55045378106, 55045378206,	

Contraceptive Method	Codes	Data Source
	55045378302, 55289024708, 55289088704, 55887005228, 55887028628, 58016474701, 58016482701, 66993061128, 66993061528, 68180084313, 68180084413, 68180084613, 68180084813, 68180085413, 68180087611, 68180087613, 68180089713, 68180089813, 68180090213, 68462030329, 68462030529, 68462030929, 68462031629, 68462031829, 68462038829, 68462039429, 68462055629, 68462056529	
Patch	HCPCS: J7304	Outpatient Services Claims Inpatient Admissions Claims
	NDC: 00062192001, 00062192015, 00062192024, 50458019201, 50458019215, 54569541300, 54868467000	Outpatient Pharmaceutical Claims
Ring	HCPCS: J7303	Outpatient Services Claims Inpatient Admissions Claims
	NDC: 00052027301, 00052027303, 54569586500, 54868483201, 55887075401	Outpatient Pharmaceutical Claims
Diaphragm	CPT: 57170 HCPCS: A4266	Outpatient Services Claims Inpatient Admissions Claims
	NDC: 00027013160, 00027013180, 00062330100, 00062330200, 00062330300, 00062330400, 00062330500, 00062330600, 00062330700, 00062330800, 00062330900, 00062331000, 00062331100, 00062331200, 00062331300, 00062334100, 00062334200, 00062334300, 00062334400, 00062334500, 00062334600, 00062334700, 00062334800, 00062334900, 00062335000, 00062335100, 00062335200, 00062338100, 00062338200, 00062338300, 00062338400, 00062338500, 00062338600, 00062338700, 00062338800, 00062338900, 00062364103, 00062364300, 00234005100, 00234013100, 00234013150, 00234013155, 00234013160, 00234013165, 00234013170, 00234013175, 00234013180, 00234013185, 00234013190, 00234013195, 00234013600, 00234013660, 00234013665, 00234013670, 00234013675,	Outpatient Pharmaceutical Claims

Contraceptive Method	Codes	Data Source
	00234013680, 00234013685, 00234013690, 00234013695, 00396401065, 00396401070, 00396401075, 00396401080	

Table 3. Opioid Use Disorder [3]

Description	Code Type	Codes
Opioid Use Disorder	ICD-9-CM ICD-10-CM	30400 30401 30402 30403 30470 30471 30472 30473 30550 30551 30552 30553 96500 96501 96502 96509 F1110 F11120 F11121 F11122 F11129 F1114 F11150 F11151 F11159 F11181 F11182 F11188 F1119 F1120 F1121 F11220 F11221 F11222 F11229 F1123 F1124 F11250 F11251 F11259 F11281 F11282 F11288 F1129 F1190 F11920 F11921 F11922 F11929 F1193 F1194 F11950 F11951 F11959 F11981 F11982 F11988 F1199

Table 4. Mode of Delivery [4, 5]

Description	Code Type	Codes
Cesarean Section	ICD-9-CM ICD-9-PCS ICD-10-CM ICD-10-PCS	66971 64981 64982 740 741 742 744 7499 O82 O7582 10D00Z0 10D00Z1 10D00Z2

Table 5. Psychiatric Diagnoses [6-8]

Psychiatric Diagnoses	Code Type	Codes
Depression	ICD-9-CM ICD-10-CM	29620 29625 29630 29635 3004 311 29383 29621 29622 29623 29624 29626 29631 29632 29633 29634 29636 F329 F324 F339 F3341 F341 F0630 F320 F321 F322 F323

Psychiatric Diagnoses	Code Type	Codes
		F325 F330 F331 F332 F333 F3342
Anxiety	ICD-9-CM ICD-10-CM	30000 30009 30020 30029 3003 F419 F418 F409 F40218 F40240 F40241 F408 F42
Post-Traumatic Stress Disorder	ICD-9-CM ICD-10-CM	30981 F4310 F4312
Bipolar Disorder	ICD-9-CM ICD-10-CM	29600 29601 29602 29603 29604 29605 29606 29610 29611 29612 29613 29614 29615 29616 29640 29641 29642 29643 29644 29645 29646 29650 29651 29652 29653 29654 29655 29656 29660 29661 29662 29663 29664 29665 29666 2967 29680 29681 29682 29689 30113 F3010 F3011 F3012 F3013 F302 F303 F304 F3110 F3111 F3112 F3113 F312 F3173 F3174 F3130 F3131 F3132 F314 F315 F3175 F3176 F3160 F3161 F3162 3163 F3164 F3177 F3178 F319 F308 F328 F3181 F340
Schizophrenia	ICD-9-CM ICD-10-CM	29500 29501 29502 29503 29504 29505 29510 29511 29512 29513 29514 29515 29520 29521 29522 29523 29524 29525 29530 29531 29532 29533 29534 29535 29540 29541 29542 29543 29544 29545 29550 29551 29552 29553 29554 29555 29560 29561 29562 29563 29564 29565 29570 29571 29572 29573 29574 29575 29580 29581 29582 29583 29584 29585 29590 29591 29592 29593 29594 29595 F2089 F201 F202 F200 F2081 F205 F259 F209

Table 6. Non-Opioid Substance Use Disorders [8]

Non-Opioid Substance Use Disorder	Code Type	Codes
Alcohol Use Disorder	ICD-9-CM ICD-10-CM	2910 2911 2912 2913 2914 2915 29181 29182 29189 2919 30300 30301 30302 30303 30390 30391 30392 30393 30500 30501 30502

Non-Opioid Substance Use Disorder	Code Type	Codes
		F1010 F10120 F10121 F10129 F1014 F10150 F10151 F10159 F10180 F10181 F10182 F10188 F1019 F1020 F1021 F10220 F10221 F10229 F10230 F10231 F10232 F10239 F1024 F10250 F10251 F10259 F1026 F1027 F10280 F10281 F10282 F10288 F1029 F10920 F10921 F10929 F1094 F10950 F10951 F10959 F1096 F1097 F10980 F10981 F10982 F10988 F1099
Drug-Induced Mental Disorders	ICD-9-CM	2920 29211 29212 2922 29281 29282 29283 29284 29285 29289 2929
Sedative, Hypnotic, or Anxiolytic Dependence	ICD-9-CM ICD-10-CM	30410 30411 30412 30413 30540 30541 30542 30543 F1310 F13120 F13121 F13129 F1314 F13150 F13151 F13159 F13180 F13191 F13182 F13188 F1319 F1320 F1321 F13220 F13221 F13229 F13230 F13231 F13232 F13239 F1324 F13250 F13251 F13259 F1326 F1327 F13280 F13281 F13282 F13288 F1329 F1390 F13920 F13921 F13929 F13930 F13931 F13932 F13939 F1394 F13950 F13951 F13959 F1396 F1397 F13980 F13981 F13982 F13988 F1399
Cocaine Dependence	ICD-9-CM ICD-10-CM	30420 30421 30422 30423 30560 30561 30562 30563 F1410 F14120 F14212 F14122 F14129 F1414 F14150 F14151 F14159 F14180 F14181 F14182 F14188 F1419 F1420 F1421 F14220 F14221 F14222 F14229 F1423 F1424 F14250 F14251 F14259 F14280 F14281 F14282 F14288 F1429 F1490 F14920 F14921 F14929 F1494 F14950

Non-Opioid Substance Use Disorder	Code Type	Codes
		F14951 F14959 F14980 F14981 F14982 F14988 F1499
Cannabis Dependence	ICD-9-CM ICD-10-CM	30430 30431 30432 30433 30520 30521 30522 30523 F1210 F12120 F12121 F12122 F121219 F12150 F12151 F12159 F12180 F12188 F1219 F1220 F1221 F12220 F12221 F12222 F12229 F12250 F12251 F12259 F12280 F12288 F1229 F1290 F12920 F12921 F12922 F12929 F12950 F12951 F12959 F12980 F12988 F1299
Amphetamine and other Psychostimulant Dependence	ICD-9-CM ICD-10-CM	30440 30441 30442 30443 30570 30571 30572 30573 F1510 F15120 F15121 F15122 F15129 F1514 F15150 F15151 F15159 F15180 F15181 F15182 F15188 1519 F1520 F1521 F15220 F15221 F15222 F15229 F1523 F1524 F15250 F15251 F15259 F15280 F15281 F15282 F15288 F1529 F1590 F15920 F15921 F15922 F15929 F1593 F1594 F15950 F15951 F15959 15980 F15981 F15982 F15988 F1599
Hallucinogen Dependence	ICD-9-CM ICD-10-CM	30450 30451 30452 30453 30530 30531 30532 30533 F1610 F16120 F16121 F16122 F16129 F1614 F16150 F16151 F16159 F16180 F16183 F16188 F1619 F1620 F1621 F16220 F16221 F16229 F1624 F16250 F16251 F16259 F16280 F16283 F16288 F1629 F1690 F16920 F16921 F16929 F1694 F16950 F16951 F16959 F16980 F16983 F16988 F1699
Other Specified Drug Dependence	ICD-9-CM ICD-10-CM	30460 30461 30462 30463 30580 30581 30582 30583

Non-Opioid Substance Use Disorder	Code Type	Codes
		F1810 F18120 F18121 F18129 F1814 F18150 F18151 F18159 F1817 F18180 F18188 F1819 F1820 F1821 F18220 F18221 F18229 F1824 F18250 F18251 F18259 F1827 F18280 F18288 F1829 F1890 F18920 18921 F18929 F1894 F18950 F18951 F18959 F1897 F18980 F18988 F1899 F1910 F19120 F19121 F19122 F1914 F19150 F19151 F19159 F1916 F1917 F19180 F19181 F19182 F19188 F1919 F1920 F1921 F19220 F19221 F19222 F19229 F19230 F19231 F19232 F19239 F1924 F19250 F19251 F19259 F1926 F1927 F19280 F19281 F19282 F19288 F1929 F1990 F19920 F19921 F19922 F19929 F19930 F19931 F19932 F19939 F1994 F19950 F19951 F19959 F1996 F1997 F19981 F19982 F19988 F1999
Combinations of Drug Dependence Excluding Opioid Type Drug	ICD-9-CM	30480 30481 30482 30483
Unspecified Drug Dependence	ICD-9-CM	30490 30491 30492 30493 30590 30591 30592 30593
Drug Dependence complicating pregnancy, childbirth, or puerperium	ICD-9-CM ICD-10-CM	64830 64831 64832 64833 64834 O99320 O99321 O99322 O99323 O99324 O99325
Noxious Influences affecting fetus or newborn via placenta or breastmilk	ICD-9-CM	76075
Drug withdrawal syndrome in newborn	ICD-9-CM ICD-10-CM	7795 P0441 P961 P962
Counseling on substance use and abuse	ICD-9-CM ICD-10-CM	V6542 Z7151

Table 7. Chronic Conditions [9-12]

Chronic Condition	Code Type	Codes
Autoimmune Disease	ICD-9-CM ICD-10-CM	1303 1361 2420 2830 340 3570 3581 35800 35801 37940 37941 37942 37943 37945 37946 37949 390 3910 3911 3912 3918 3919 393 4290 4460 4461 4464 4467 5472 5790 5813 5819 5830 5831 5832 5833 5834 6940 6942 6943 6944 6945 6960 6961 7010 7101 3920 3929 3940 3941 3942 3949 3950 3951 3952 3959 3960 3961 3962 3963 3968 3969 3970 3971 3979 3980 39890 39891 39899 4220 42290 42291 42292 42293 42299 44620 44621 44629 51630 51631 51362 51633 51634 51635 51636 51637 5171 5172 5173 5178 5550 5551 5552 5559 5560 5561 5562 5563 5564 5565 5566 5568 5569 5800 5804 58081 58089 5809 5820 5821 5822 5824 58281 58289 5829 69460 69461 71430 71431 71432 71433 85110 85111 85112 85113 85114 85115 85116 85119 7100 7103 7104 7140 7141 7142 7200 B5881 M352 D590 D591 G35 G610 G733 I00 I092 I514 M300 M303 M3130 M314 K900 N040 N049 N059 N052 N055 L130 L122 L401 L100 L101 L102 L104 L109 L120 L128 L4054 L4059 L400 L401 L402 L403 L404 L408 L900 L940 L943 M340 M341 M349 M3210 M3390 M3320 M069 M0500 M0530 M0560 M061 M459 E0590 E0591 E0500 E0501 E0510 E0511 E0520 E0521 E0530 E0531 E0540 E0541 E0580 E0581 G7000 G7001 H5700 H5701 H5702 H5703 H5704 H5709 I010 I011 I012 I018 I019 I010 I011 I012 I018

Chronic Condition	Code Type	Codes
		I019 I050 I051 I052 I058 I059 I060 I061 I062 I068 I069 I080 I081 I082 I083 I088 I089 I070 I071 I072 I078 I079 I090 I091 I092 I0981 I0989 I099 I41 I409 I400 I401 I408 M310 J84111 J84112 J84113 J84114 J85115 J842 J85117 J17 M3481 J99 K5000 K5010 K5080 K5090 K5180 K5120 K5130 K5140 K5150 K5100 K5190 N003 N013 N009 N08 N008 N032 N033 N035 N038 N039 N08 N038 L121 M0800 M083 M0840 S0190XA S06330A S06332A S06333A S06334A S06335A S06336A S06337A S06339A
Chronic Hypertension	ICD-9-CM ICD-10-CM	64200 64201 64202 64203 64204 64210 64211 64212 64213 64214 64220 64221 64222 64223 64224 64290 64291 64292 64293 64294 64270 64271 64272 64273 64274 4010 4011 4019, 40501 40509 40511 40519 40591 40599 4160 45930 45931 45932 45933 45939 O10011 O10012 O10013 O10019 O1002 O1003 O10111 O10112 O10113 O10119 O1012 O1013 O10211 O10212 O10213 O10219 O1022 O1023 O10311 O10312 O10313 O10319 O1032 O1033 O10411 O10412 O10413 O10419 O1042 O1043 O10911 O10912 O10913 O10919 O1092 O1093 O161 O162 O163 O169 0111 O112 O113 O119 I10 I150 I158 I270 I87309 I87319 I87329 I87339 I87399
Gestational Hypertension	ICD-9-CM ICD-10-CM	64230 64231 64232 64233 64234 64240 64241 64242 64243 64244 64250 64251 64252 64253 64254 64260 6426164262 64263 64264 0131

Chronic Condition	Code Type	Codes
		O132 O139 01400 O1402 O1403 O1410 O1412 O1413 O1420 O1422 O1423 O1490 O1492 O1493 01500 O1502 O1503 O151 O152 O159
Diabetes Miletus	ICD-9-CM ICD-10-CM	25000 25001 25002 25003 25010 25011 25012 25013 25020 25021 25022 25023 25030 25031 25032 25033 25040 25041 25042 25043 25050 25051 25052 25053 25060 25061 25062 25063 25070 25071 25072 25073 25080 25081 25082 25083 25090 25091 25092 25093 24900 24901 24910 24911 24920 24921 24930 24931 24940 24941 24950 24951 24960 24961 24970 24971 24980 24981 24990 24991, 36201 36202 36203 36204 36205 36206 36207, 36641, 3572, 64800 64801 64802 64803 64804 O24011 O24012 O24013 O24019 O2402 O2403 O24111 O24112 O24113 O24119 O2412 O2413 O24311 O24312 O24313 O24319 O2432 O2433 O24811 O24812 O24813 O24819 O2482 O2483 O24911 O24912 O24913 O24919 O2492 O2493 E0800 E0801 E0821 E0822 E0829 E0840 E0841 E0842 E0843 E0844 E0849 E0851 E0852 E0859 E088 E089 E08311 E08319 E08321 E08329 E08331 E08339 E08341 E08349 E08351 E08359 E0836 E0839 E08610 E08618 E08620 E08621 E08622 E08628 E08630 E08638 E08641 E08649 E0900 E0901 E0910 E0911 E0921 E0922 E0929 E0940 E0941 E0942 E0943 E0944 E0949 E0951 E0952 E0959 E098 E099 E09311 E09319 E09321 E09329 E09331 E09339 E09341 E09349

Chronic Condition	Code Type	Codes
		E09351 E09359 E0936 E0939 E09610 E09618 E09620 E09621 E09622 E09628 E09630 E09638 E09641 E09649 E0965 E0969 E1010 E1011 E1021 E1022 E1029 E1040 E1041 E1042 E1043 E1044 E1049 E1051 E1052 E1059 E108 E109 E10311 E10319 E10321 E10329 E10331 E10339 E10341 E10349 E10351 E10359 E1036 E1039 E10610 E10618 E10620 E10621 E10622 E10628 E10630 E10638 E10641 E10649 E1065 E1069 E1100 E1101 E1121 E1122 E1129 E1140 E1141 E1142 E1143 E1144 E1149 E1151 E1152 E1159 E118 E119 E11311 E11319 E11321 E11329 E11331 E11339 E11341 E11349 E11351 E11359 E1136 E1139 E11610 E11618 E11620 E11621 E11622 E11628 E11630 E11638 E11641 E11649 E1165 E1169 E1300 E1301 E1310 E1311 E1321 E1322 E1329 E1340 E1341 E1342 E1343 E1344 E1349 E1351 E1352 E1359 E138 E139 E13311 E13319 E13321 E13329 E13331 E13339 E13341 E13349 E13351 E13359 E1336 E1339 E13610 E13618 E13620 E13621 E13622 E13628 E13630 E13638 E13641 E13649 E1365 E1369
Gestational Diabetes	ICD-9-CM ICD-10-CM	64880 64881 64882 64883 64884 O24410 O24414 O24419 O24420 O24424 O24429 O24430 O24434 O24439
Asthma	ICD-9-CM ICD-10-CM	49300 49301 49302 49310 49311 49312 49320 49321 49322 49381 49382 49390 49391 49392 J4520 J4521 J4522 J4530 J4531 J4532 J4540 J4541 J4542 J4550

Chronic Condition	Code Type	Codes
		J4551 J4552 J45901 J45902 J45909 J45990 J45991 J45998
Hepatitis C	ICD-9-CM ICD-10-CM	07041 07044 07051 07054 0707 07070 07071 B182 B1711 B1710 B182 B1920 B1921

Table 8. Pain Conditions [13]

Pain Condition	Code Type	Codes
Back Pain	ICD-9-CM ICD-10-CM	72130 72142 72252 72273 72402 72403 72420 72430 72440 72450 M4306 M4307 M4316 M4317 M4716 M4726 M4727 M47816 M47817 M47896 M47897 M4806 M4807 M5106 M5116 M5117 M5126 M5127 M5136 M5137 M5416 M5417 M5430 M5431 M5432 M5440 M5441 M5442 M545 M5489 M549 S39012A S39012D S39012S S39023A S39023D S39023S S39092A S39092D S39092S
Headache	ICD-9-CM ICD-10-CM	30781 33900 33901 33902 33903 33904 33905 33909 33910 33911 33912 33920 33921 33922 3393 33941 33942 33943 33944 33981 33982 33983 33984 33985 33989 3490 7238 7840 3490 3491 3492 34931 34939 34981 34982 34989 3499 R51 G971 M5481 G43001 G43009 G43011 G43019 G43101 G43109 G43111 G43119G43401 G43409 G43411 G43419 G43501 G43509 G43511 G43519 G43601 G43609 G43611 G43619 G43701 G43709 G43711 G43719 G43A0 G43A1 G43B0 G43B1 G43C0 G43C1 G43D0 G43D1 G43801 G43809 G43811 G43819 G43821 G43829 G43831 G43839 G43901 G43909 G43911 G43919 G44001 G44009 G44011 G44019 G44021

Pain Condition	Code Type	Codes
		G44029 G44031 G44039 G44041 G44049 G44051 G44059 G44091 G44099 G441 G44201 G44209 G44211 G44219 G44221 G44229 G44301 G44309 G44311 G44319 G44321 G44329 G4440 G4441 G4451 G4452 G4453 G4459 G4481 G4482 G4483 G4484 G4485 G4489
Fibromyalgia	ICD-9-CM ICD-10-CM	7291 M797
Arthritis	ICD-9-CM ICD-10-CM	140 7141 7142 71430 71431 71432 71433 7144 71481 71489 7149 71500 71504 71509 71510 71511 71512 71513 71514 71515 71516 71517 71518 71520 71521 71522 71523 71524 71525 71526 71527 71528 71530 71531 71532 71533 71534 71535 71536 71537 71538 71580 71589 71590 71591 71592 71593 71594 71595 71596 71597 71598 M0500 M05011 M05012 M05019 M05021 M05022 M05029 M05031 M05032 M05039 M05041 M05042 M05049 M05051 M05052 M05059 M05061 M05062 M05069 M05071 M05072 M05079 M0509 M0510 M05111 M05112 M05119 M05121 M05122 M05129 M05131 M05132 M05139 M05141 M05142 M05149 M05151 M05152 M05159 M05161 M05162 M05169 M05171 M05172 M05179 M0519 M0520 M05211 M05212 M05219 M05221 M05222 M05229 M05231 M05232 M05239 M05241 M05242 M05249 M05251 M05252 M05259 M05261 M05262 M05269

Pain Condition	Code Type	Codes
		M05271 M05272 M05279 M0529 M0530 M05311 M05312 M05319 M05321 M05322 M05329 M05331 M05332 M05339 M05341 M05342 M05349 M05351 M05352 M05359 M05361 M05362 M05369 M05371 M05372 M05379 M0539 M0540 M05411 M05412 M05419 M05421 M05422 M05429 M05431 M05432 M05439 M05441 M05442 M05449 M05451 M05452 M05459 M05461 M05462 M05469 M05471 M05472 M05479 M0549 M0550 M05511 M05512 M05519 M05521 M05522 M05529 M05531 M05532 M05539 M05541 M05542 M05549 M05551 M05552 M05559 M05561 M05562 M05569 MO5571 MO5572 MO5579 MO559 M0560 M05611 M05612 M05619 MO5621 MO5622 M05629 M05631 M05632 M05639 M05641 M05642 M05649 M05651 M05652 M05659 M05661 M05662 M05669 M05671 M05672 M05679 M0569 M0570 M05711 M05712 M05719 M05721 M05722 M05729 M05731 M05732 M05739 M05741 M05742 M05749 M05751 M05752 M05759 M05761 M05762 M05769 M05771 M05772 M05779 M0579 M0580 M05811 M05812 M05819 M05821 M05822 M05829 M05831 M05832 M05839 M05841 M05842 M05849 M05851 M05852 M05859 M05861 M05862 M05869 M05871 M05872 M05879

Pain Condition	Code Type	Codes
		M0589 M059 M0600 M06011 M06012 M06019 M06021 M06022 M06029 M06031 M06032 M06039 M06031 M06032 M06039 M06041 M06042 M06049 M06051 M06052 M06059 M06061 M06062 M06069 M06071 M06072 M06079 M0608 M0609 M061 M0620 M06221 M06212 M06219 M06221 M06222 M06229 M06231 M06232 M06239 M06241 M06242 M06249 M06251 M06252 M06259 M06261 M06262 M06269 M06271 M06272 M06279 M0628 M0629 M0630 M06311 M06312 M06319 M06321 M06322 M06329 M06331 M06332 M06339 M06341 M06342 M06349 M06351 M06352 M06359 M06361 M06362 M06369 M06371 M06372 M06379 M0638 M0639 M064 M0680 M06811 M06812 M06819 M06821 M06822 M06829 M06831 M06832 M06839 M06841 M06842 M06849 M06851 M06852 M06859 M06861 M06862 M06869 M06871 M06872 M06879 M0688 M0689 M069 M150 M151 M152 M153 M154 M158 M159 M160 M1610 M1611 M1612 M162 M1630 M1631 M1632 M164 M1650 M1651 M1652 M166 M167 M169 M170 M1710 M1711 M1712 M172 M1730 M1731 M1732 M174 M175 M179 M180 M1810 M1811 M1812 M182 M1830 M1831 M1832 M184 M1850 M1851 M1852 M189 M19011 M19012 M19019 M19021

Pain Condition	Code Type	Codes
		M19022 M19029 M19031 M19032 M19039 M19041 M19041 M19049 M19071 M19072 M19079 M19111 M19112 M19119 M19121 M19122 M19129 M19131 M19132 M19139 M19141 M19142 M19149 M19171 M19172 M19179 M19211 M19212 M19219 M19221 M19222 M19229 M19231 M19232 M19239 M19241 M19242 M19249 M19271 M19272 M19279 M1990 M1991 M1992 M1993
Neuropathic Pain	ICD-9-CM ICD-10-CM	05312 05313 3501 3502 3508 3509 3530 3531 3532 3533 3534 3535 3536 3538 3539 3540 3541 3542 3543 3544 3545 3548 3549 3550 3551 3552 3553 3554 3556 35571 35579 3558 3559 3560 3561 3562 3563 3564 3568 3569 33720 33721 33722 33729 25060 25061 25062 25063 G500 G501 G508 G509 G510 G511 G512 G513 G514 G518 G519 G520 G521 G522 G523 G527 G528 G529 G53 G540 G546 G548 G59 G600 G601 G602 G603 G608 G609 B0222 B0223 B0229 G9050 G90511 G90512 G90513 G90519 G90521 G90522 G90523 G90529 G9059 E1340 E1342 E1342 E1343 E1344 E1349

Table 9. ANC and PNC Codes and Definition [14]

Description	Code Type	Codes
Antenatal Care Visit Visit Location “medical office” or “outpatient hospital location” AND diagnosis code OR provider type	ICD-9-CM ICD-10-CM	O0900 O0901 O0902 O0903 O0910 O0911 O0912 O0913 O09211 O09212 O09213 O09219 O09291 O09292 O09293 O09299 O0930 O0931 O0932 O0933

Description	Code Type	Codes
"obstetrics & gynecology, certified nurse midwife, gynecologist, family practice, family practice OB/Gyn, certified nurse midwife, maternal and fetal medicine, nurse practitioner, or perinatology"		O0940 O0941 O0942 O0943 O09511 O09512 O09513 O09519 O09521 O09522 O09523 O09529 O09611 O09612 O09613 O09619 O09621 O09622 O09623 O09629 O0970 O0971 O0972 O0973 O09811 O09812 O09813 O09819 O09821 O09822 O09823 O09829 O09891 O09892 O09893 O09899 O0990 O0991 O0992 O0993 O3680X0 Z3400 Z3401 Z3402 Z3403 Z3480 Z3481 Z3482 Z3483 Z3490 Z3491 Z3492 Z3493 V220 V221 V230 V231 V232 V233 V2341 V2342 V2349 V235 V237 V2381 V2382 V2384 V2385 V2386 V2387 V2389 V239
Postpartum Care Visit Visit Location "medical office" or "outpatient hospital location" AND diagnosis code OR provider type "obstetrics & gynecology, certified nurse midwife, gynecologist, family practice, family practice OB/Gyn, certified nurse midwife, maternal and fetal medicine, nurse practitioner, or perinatology"	ICD-9-CM ICD-10-CM	V241 V242 Z391 Z392

Table 10. NAS Diagnosis [3, 15-17]

Description	Code Type	Codes
Neonatal Abstinence Syndrome	ICD-9-CM ICD-10-CM	779.5 76072 P96.1, P0449
Conditions Associated with Iatrogenic Neonatal Abstinence Syndrome (Exclusionary Codes)		
Very Low Birthweight	ICD-9-CM ICD-10-CM	V2131, V2132 P07.00, P07.02, P07.01, P07.03
Intraventricular Hemorrhage	ICD-9-CM ICD-10-CM	772.10, 772.12, 772.14, 772.11, 772.13 P523, P521, P5222, P520, P5221
Periventricular Leukomalacia	ICD-9-CM ICD-10-CM	779.7 P91.2
Necrotizing Enterocolitis	ICD-9-CM ICD-10-CM	777.51, 777.52, 777.53, 777.50 P779, P773, P772, P771

Description	Code Type	Codes
Spontaneous Intestinal Perforation	ICD-9-CM ICD-10-CM	777.6 P78.0
Bronchopulmonary Dysplasia	ICD-9-CM ICD-10-CM	770.7 P27.0, P27.1, P27.8

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Appendix B

Characteristics of Aim 1 Cohort by Provision of Immediate Postpartum Prescription Contraception within Three days Postpartum, Row Totals

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	MEM
Total N (%)	1,204,405 (93.3%)	86,947 (6.7%)	72,582 (5.6%)	1,331 (0.1%)	13,034 (1.0%)
Opioid Use					
No Opioid Use During Pregnancy	93.6% (1,093,024)	6.4% (74,204)	5.2% (61,306)	0.1% (1,184)	1.0% (11,714)
Non-Chronic Prescription Opioid Use	90.0% (98,661)	10.0% (10,961)	8.8% (9,691)	0.1% (111)	1.1% (1.159)
Chronic Prescription Opioid Use	85.4% (7,979)	14.6% (1,368)	13.5% (1,263)	0.2% (14)	1.0% (91)
OUD Diagnosis/ Buprenorphine Prescription	92.0% (4,741)	8.0% (414)	6.2% (322)	0.4% (22)	1.4% (70)
Age, mean years (SD)	30.1 (5.4)	32.8 (5.1)	33.6 (4.7)	28.9 (6.1)	28.8 (5.2)
Age, Categorical					
<20	98.3% (36,274)	1.6% (608)	0.02% (9)	0.2% (83)	1.4% (516)
20-24	97.0% (154,366)	3.0% (4,830)	1.4% (2,307)	0.2% (264)	1.4% (2,259)
25-29	95.3% (339,717)	4.6% (16,582)	3.3% (11,861)	0.1% (352)	1.2% (4,369)
30-34	93.2% (424,558)	6.8% (30,857)	5.8% (26,309)	0.1% (380)	0.9% (4,168)
35-39	88.6% (202,060)	11.4% (25,886)	10.6% (24,197)	0.1% (204)	0.6% (1,485)
40+	85.3% (47,430)	14.7% (8,184)	14.2% (7,899)	0.1% (48)	0.4% (237)
HRSA Region					
Region 1	95.4% (53,217)	4.6% (2,565)	3.6% (2,032)	0.1% (53)	0.9% (480)
Region 2	95.7% (93,105)	4.3% (4,177)	3.9% (3,760)	0.1% (83)	0.3% (334)
Region 3	93.4% (104,132)	6.6% (7,382)	5.3% (5,962)	0.1% (127)	1.2% (1,293)
Region 4	91.6% (256,850)	8.4% (23,620)	7.3% (20,580)	0.1% (264)	1.0% (2,776)
Region 5	94.4% (223,700)	5.6% (13,220)	4.6% (10,864)	0.1% (299)	0.9% (2,057)
Region 6	91.5% (156,413)	8.4% (14,432)	7.6% (12,951)	0.1% (150)	0.8% (1,331)
Region 7	93.6% (49,364)	6.4% (3,362)	5.0% (2,619)	0.1% (58)	1.3% (685)
Region 8	93.6% (38,456)	6.4% (2,648)	4.4% (1,793)	0.04% (18)	2.0% (837)
Region 9	94.0% (145,816)	6.0% (9,367)	4.5% (6,948)	0.1% (202)	1.4% (2,217)

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	MEM
Region 10	93.6% (48,522)	6.4% (3,309)	4.9% (2,567)	0.1% (51)	1.3% (691)
Unknown	92.4% (34,830)	7.6% (2,865)	6.6% (2,506)	0.1% (26)	0.9% (333)
Delivery in State with ≥20% Hispanic Population					
Yes	93.0% (353,578)	7.0% (26,690)	5.9% (22,634)	0.1% (321)	1.0% (3,735)
No	93.4% (850,827)	6.6% (60,257)	5.5% (49,948)	0.1% (1,010)	1.0% (9,299)
Delivery in State with ≥20% Black Population					
Yes	91.5% (196,453)	8.5% (18,313)	7.4% (15,886)	0.1% (329)	1.0% (2,098)
No	93.6% (1,007,952)	6.4% (68,634)	5.5% (49,948)	0.1% (1,010)	1.0% (9,299)
Delivery in State with ≥15% Population in Poverty					
Yes	91.0% (158,883)	9.0% (15,665)	7.6% (13,306)	0.2% (281)	1.2% (2,078)
No	93.6% (1,045,522)	6.4% (71,282)	5.3% (59,276)	0.1% (1,050)	1.0% (10,956)
Delivery in State with ≥35% Women with College Degree or More					
Yes	94.8% (123,851)	5.2% (6,772)	4.3% (5,636)	0.1% (116)	0.8% (1,020)
No	93.1% (1,080,554)	6.9% (80,175)	5.8% (66,946)	0.1% (1,215)	1.0% (12,014)
Insurance Plan Type					
PPO	93.3% (716,215)	6.7% (51,300)	5.7% (44,083)	0.1% (708)	0.8% (6,509)
Comprehensive	93.7% (12,290)	6.3% (832)	5.0% (662)	0.2% (28)	1.1% (142)
HMP/EPO	92.9% (176,389)	7.1% (13,453)	5.1% (9,748)	0.2% (299)	1.8% (3,406)
POS	92.8% (87,604)	7.2% (6,840)	6.2% (5,841)	0.1% (112)	0.9% (887)
CDHP	93.7% (98,755)	6.3% (6,690)	5.5% (5,775)	0.1% (92)	0.8% (823)
HDHP	94.3% (73,872)	5.7% (4,430)	4.8% (3,773)	0.1% (68)	0.7% (589)
Unknown	92.0% (39,280)	8.0% (3,402)	6.3% (2,700)	0.1% (24)	1.6% (678)
Year of Delivery					
2011	92.5% (250,180)	7.5% (20,325)	6.4% (17,284)	0.1% (161)	1.1% (2,880)
2012	92.9% (241,621)	7.1% (18,562)	6.0% (15,686)	0.1% (199)	1.0% (2,677)
2013	93.1% (180,640)	6.9% (13,401)	5.7% (11,055)	0.1% (155)	1.1% (2,191)
2014	93.5% (170,431)	6.5% (11,784)	5.4% (9,910)	0.1% (177)	0.9% (1,697)
2015	93.9% (135,624)	6.1% (8,843)	5.1% (7,308)	0.1% (179)	0.9% (1,356)
2016	94.1% (128,925)	5.9% (8,053)	4.8% (6,538)	0.1% (206)	1.0% (1,309)
2017	94.2% (96,984)	5.8% (5,979)	4.7% (4,801)	0.2% (254)	0.9% (924)
Delivery Mode					

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	MEM
Vaginal	97.5% (811,700)	2.5% (20,623)	1.3% (10,958)	0.1% (550)	1.1% (9,115)
Cesarean Section	85.5% (392,705)	14.5% (66,324)	13.4% (61,624)	0.2% (781)	0.8% (3,919)
Non-Opioid Substance Use Disorder					
Yes	92.8% (16,319)	7.2% (1,265)	5.3% (933)	0.3% (58)	1.6% (274)
No	93.3% (1,188,086)	6.7% (85,682)	5.6% (71,649)	0.1% (1,273)	1.0% (12,760)
Psychiatric Disorder, Any					
Yes	92.0% (66,007)	8.0% (5,700)	6.4% (4,609)	0.2% (133)	1.3% (958)
No	93.3% (1,138,398)	6.7% (81,247)	5.6% (67,973)	0.1% (1,198)	1.0% (12,076)
Chronic Hypertension					
Yes	89.6% (97,249)	10.4% (11,254)	9.3% (10,052)	0.2% (185)	0.9% (1,017)
No	93.6% (1,107,156)	6.4% (75,693)	5.3% (62,530)	0.1% (1,146)	1.0% (12,017)
Gestation Hypertension					
Yes	92.4% (144,401)	7.6% (11,816)	6.5% (10,174)	0.1% (207)	0.9% (1,435)
No	93.4% (1,060,004)	6.6% (75,131)	5.5% (62,408)	0.1% (1,124)	1.0% (11,599)
Diabetes Mellitus					
Yes	88.1% (47,601)	11.9% (6,422)	10.9% (5,886)	0.2% (89)	0.8% (447)
No	93.5% (1,156,804)	6.5% (80,525)	5.4% (66,696)	0.1% (1,242)	1.0% (12,587)
Gestational Diabetes					
Yes	90.6% (168,730)	9.4% (17,560)	8.5% (15,820)	0.1% (191)	0.8% (1,549)
No	93.7% (1,035,675)	6.3% (69,387)	5.1% (56,762)	0.1% (1,140)	1.0% (11,485)
Asthma					
Yes	92.5% (58,042)	7.5% (4,676)	5.9% (3,678)	0.2% (120)	1.4% (878)
No	93.3% (1,146,363)	6.7% (82,271)	5.6% (68,904)	0.1% (1,211)	1.0% (12,156)
Autoimmune Disorder					
Yes	91.9% (22,777)	8.0% (1,992)	6.9% (1,703)	2.0% (39)	1.0% (250)
No	93.3% (1,181,628)	6.7% (84,955)	5.6% (70,879)	0.1% (1,292)	1.0% (12,784)
Hepatitis C					
Yes	91.1% (864)	8.9% (84)	6.6% (63)	1.0% (9)	1.3% (12)
No	93.3% (1,203,541)	6.7% (86,863)	5.6% (72,519)	0.1% (1,322)	1.0% (13,022)
Pain-Related Conditions					
Yes	92.2% (99,073)	7.8% (8,371)	6.6% (7,051)	0.2% (174)	1.1% (1,146)

	No Evidence of Contraception Provision	Evidence of Contraception Provision	Female Sterilization	LARC	MEM
No	93.4% (1,105,332)	6.6% (78,576)	5.5% (65,531)	0.1% (1,157)	1.0% (11,888)
Any ANC					
Yes	93.3% (1,165,495)	6.7% (84,275)	5.6% (70,467)	0.1% (1,298)	1.0% (12,510)
No	93.6% (38,910)	6.4% (2,672)	5.1% (2,115)	0.1% (33)	1.3% (524)

Appendix C

Crude Estimates of Mean Time to Contraceptive Provision in Women Who Were Provided Contraception Within 365 Postpartum, Aim 2 Cohort

Covariable	Mean Days to Contraceptive Provision (95% CI)
Opioid Use During Pregnancy	
No use	61.92 (61.76-62.08)
Non-Chronic Prescription Use	59.34 (58.84-59.82)
Chronic Prescription Use	54.88 (53.23-56.52)
OUD/BUP	72.32 (69.54-75.10)
Contraceptive Method Type	
Any Method	61.66 (61.49-61.69)
Sterilization	13.26 (12.98-13.54)
LARC	76.58 (76.30-76.86)
MEM	66.19 (65.99-66.39)
Age at Delivery	
>20	75.51 (74.64-76.38)
20-24	69.32 (68.90-69.74)
25-29	61.49 (61.23-61.76)
30-34	60.82 (60.56-61.08)
35-39	55.82 (55.41-56.23)
40+	50.54 (49,60-51.49)
HRSA Region	
Region 1	66.49 (65.74-67.25)
Region 2	72.85 (72.12-73.57)
Region 3	62.86 (62.32-63.41)
Region 4	59.91 (59.59-60.22)
Region 5	62.59 (62.23-62.94)
Region 6	58.23 (57.84-58.63)
Region 7	61.21 (60.50-61.93)
Region 8	58.31 (57.56-59.05)
Region 9	63.61 (63.14-64.09)
Region 10	57.94 (57.25-58.63)
Unknown	56.88 (56.09-57.68)
Delivery in State with ≥20% Hispanic Population	
No	61.49 (61.31-61.67)
Yes	62.02 (61.73-62.31)
Delivery in State with ≥20% Black Population	
No	62.03 (61.86-62.20)
Yes	59.82 (59.46-60.19)
Delivery in State with ≥15% Population in Poverty	

Covariable	Mean Days to Contraceptive Provision (95% CI)
No	62.32 (62.15-62.49)
Yes	57.79 (57.41-58.17)
Delivery in State with ≥35% Women with College Degree or More	
No	61.15 (60.98-61.31)
Yes	66.49 (65.97-67.01)
Insurance Plan Type	
PPO	61.59 (61.39-61.79)
Comprehensive	65.40 (63.71-67.10)
HMO/EPO	61.37 (60.97-61.77)
POS/POS + Capitation	63.16 (62.59-63.73)
CDHP	62.49 (61.93-63.04)
HDHP	62.08 (61.41-62.74)
Unknown	56.68 (55.89-57.47)
Year of Delivery	
2011	64.11 (63.78-64.45)
2012	61.30 (60.98-61.63)
2013	60.88 (60.51-61.25)
2014	58.94 (58.57-59.30)
2015	62.37 (61.92-62081)
2016	61.31 (60.86-61.77)
Delivery Mode	
Vaginal	67.58 (67.39-67.78)
Cesarean Section	52.11 (51.86-52.35)
Non-Opioid Substance Use Disorder	
No	61.55 (61.39-61.70)
Yes	67.97 (66.56-69.37)
Psychiatric Disorder, Any	
No	61.59 (61.43-61.75)
Yes	62.50 (61.85-63.15)
Chronic Hypertension	
No	62.21 (61.96-62.28)
Yes	56.76 (56.26-57.26)
Gestational Hypertension	
No	61.87 (61.71-62.04)
Yes	60.09 (59.67-60.50)
Diabetes Mellitus	
No	61.91 (61.75-62.06)
Yes	55.61 (54.85-56.37)
Gestational Diabetes	
No	62.26 (62.10-62.43)
Yes	57.97 (57.57-58.38)

Covariable		Mean Days to Contraceptive Provision (95% CI)
Asthma		
	No	61.65 (61.49-61.81)
	Yes	61.47 (60.79-62.15)
Autoimmune Disease		
	No	61.66 (61.50-61.81)
	Yes	60.89 (59.75-62.04)
Pain Condition		
	No	61.68 (61.52-61.84)
	Yes	61.18 (60.63-61.74)
Hepatitis C		
	No	61.64 (61.49-61.79)
	Yes	63.37 (57.31-69.42)
Any ANC		
	No	61.54 (60.66-62.42)
	Yes	61.64 (61.49-61.80)

Appendix D

Log-Rank Test Results from Kaplan-Meier Curves for all Categorical Covariates in Aim 2 Analysis

Variables	Events Observed	Events Expected	P-Value
Opioid Use			<0.001
No Opioid Use During Pregnancy	565,692	577,757.79	
Non-Chronic Prescription Opioid Use	63,919	53,233.95	
Chronic Prescription Opioid Use	5,713	4,432.52	
OUD Diagnosis/Buprenorphine Prescription	2,694	2,593.74	
Maternal Age			<0.001
<20	22,568	18,157.12	
20-24	90,532	76,488.87	
25-29	188,342	171,622.94	
30-34	217,639	227,000.84	
35-39	98,331	115,539.71	
40+	20,606	29,208.52	
HRSA Region			<0.001
Region 1	26,338	29,447.33	
Region 2	36,463	53,325.61	
Region 3	52,701	56,667.58	
Region 4	148,128	127,883.83	
Region 5	115,354	120,113.98	
Region 6	91,566	79,752.13	
Region 7	27,975	25,049.80	
Region 8	22,059	19,843.31	
Region 9	70,571	81,916.13	
Region 10	26,795	24,815.36	
Unknown	20,068	19,202.94	
Delivery in State with ≥20% Hispanic Population			<0.001
No	455,849	446,810.45	
Yes	182,169	191,207.55	
Delivery in State with ≥20% Black Population			<0.001
No	524,912	540,840.40	
Yes	113,106	97,177.60	

Variables	Events Observed	Events Expected	P-Value
Delivery in State with ≥15% Population in Poverty			<0.001
No	542,370	560,323.29	
Yes	95,640	77,694.71	
Delivery in State with ≥35% Women with College Degree or More			<0.001
No	578,879	569,776.34	
Yes	59,139	68,241.66	
Insurance Plan Type			<0.001
PPO	384,466	382,861.98	
Comprehensive	5,888	5,919.29	
HMO/EPO	95,078	95,795.80	
POS/POS + Capitation	47,917	46,486.33	
CDHP	49,572	48,675.79	
HDHP	33,747	36,788.53	
Unknown	21,350	21,490.28	
Year of Delivery			
2011	146,132	144,079.32	
2012	141,283	139,792.35	
2013	106,313	102,928.90	
2014	98,155	98,306.95	
2015	76,174	78,264.73	
2016	69,961	74,645.75	
Delivery Mode			<0.001
Vaginal	393,075	427,846.46	
Cesarean Section	244,943	210,171.54	
Non-Opioid Substance Use Disorder			<0.001
No	628743	629641.68	
Yes	9275	8376.32	
Psychiatric Disorder, Any			<0.001
No	600388	603932.25	
Yes	37630	34085.75	
Chronic Hypertension			<0.001
No	580,660	587,620.01	
Yes	57,358	50,397.99	
Gestational Hypertension			<0.001
No	555,961	563,193.68	
Yes	82,057	74,824.32	
Diabetes Mellitus			0.03

Variables	Events Observed	Events Expected	P-Value
No	611,154	611,487.64	
Yes	26,864	26,530.36	
Gestational Diabetes			0.01
No	545,390	544,668.86	
Yes	92,628	93,349.14	
Asthma			<0.001
No	605,638	608,515.55	
Yes	32,380	29,502.45	
Autoimmune Disease			0.24
No	626,126	626,000.99	
Yes	11,892	12,017.01	
Pain Condition			<0.001
No	581,171	590,419.12	
Yes	50,847	47,598.88	
Hepatitis C			0.49
No	637,600	637,585.87	
Yes	418	432.13	
Any ANC			<0.001
No	19,429	22,419.30	
Yes	618,589	615,598.70	

Appendix E

Aim 2 Kaplan-Meier Curve Graphs and Log-Log Plots

Figure 1. Opioid Use During Pregnancy Kaplan-Meier Survival Curve Estimates

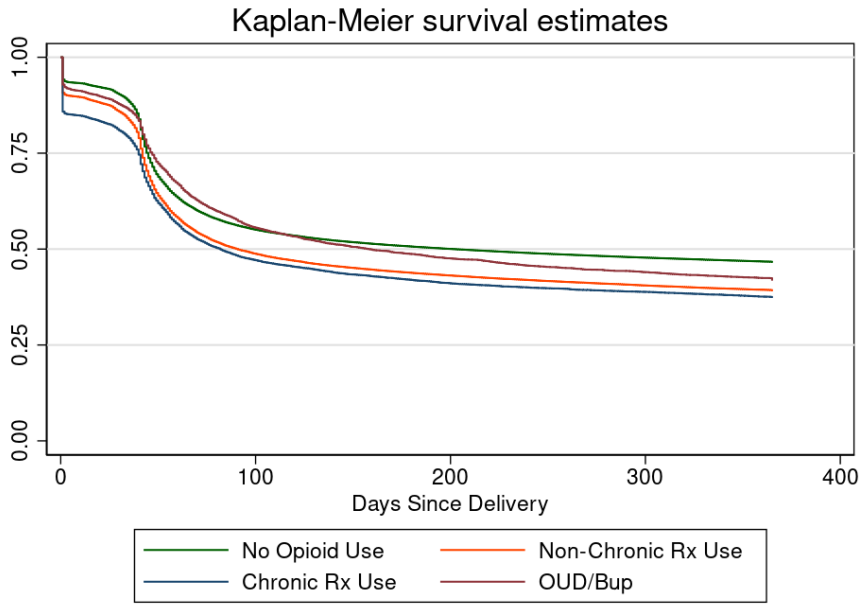


Figure 2. Maternal Age Kaplan-Meier Survival Curve Estimates

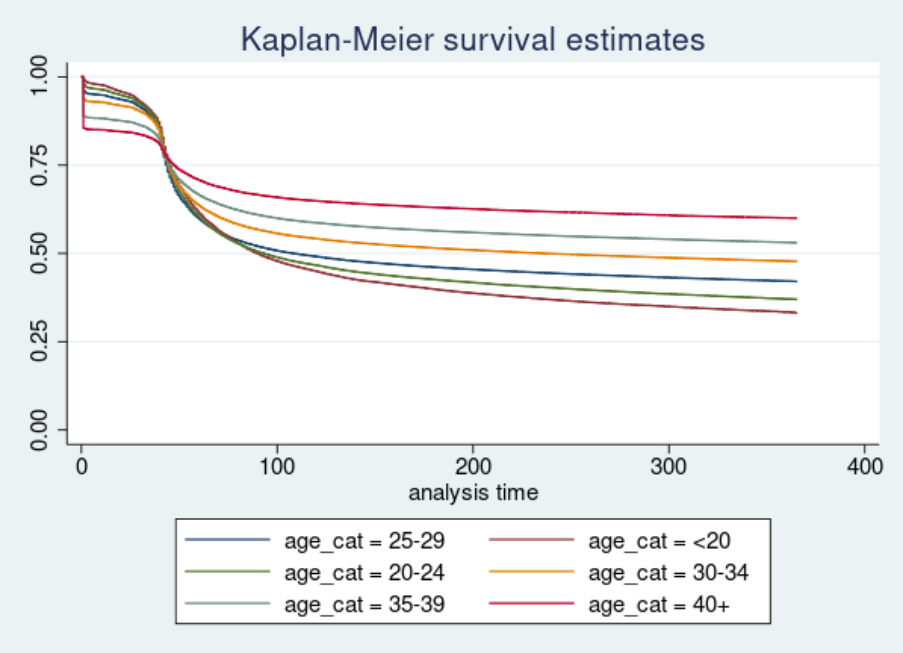


Figure 3. HRSA Region Kaplan-Meier Survival Curve Estimates

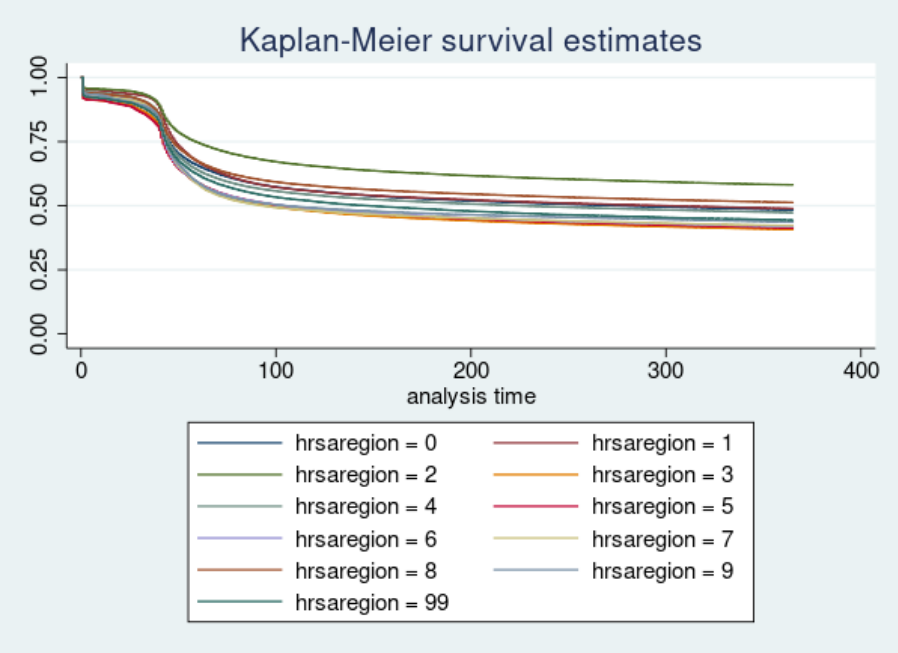


Figure 4. Delivery in State with ≥20% Hispanic Population Kaplan-Meier Survival Curve Estimates

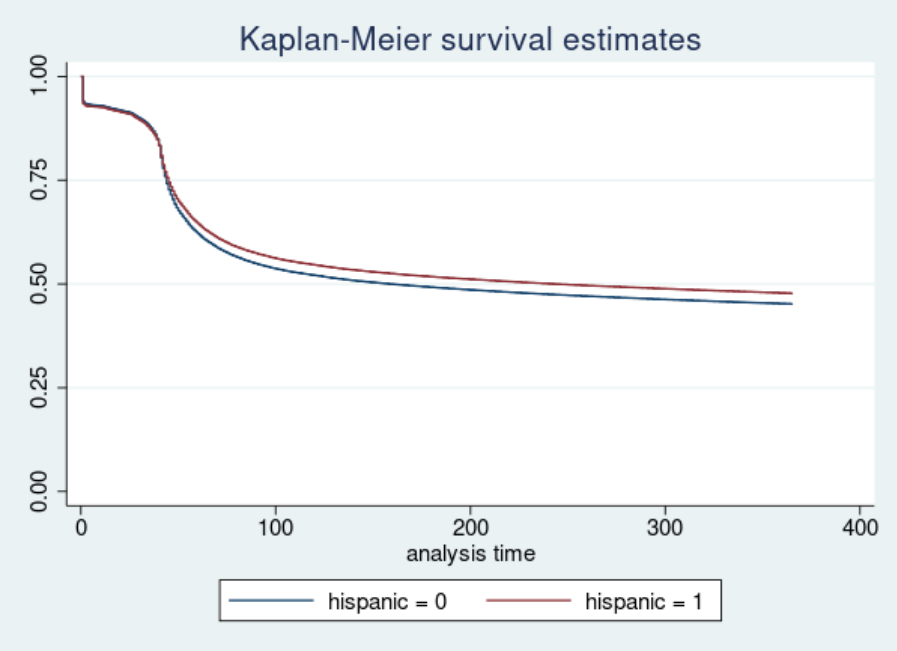


Figure 5. Delivery in State with ≥20% Black Population Kaplan-Meier Survival Curve Estimates

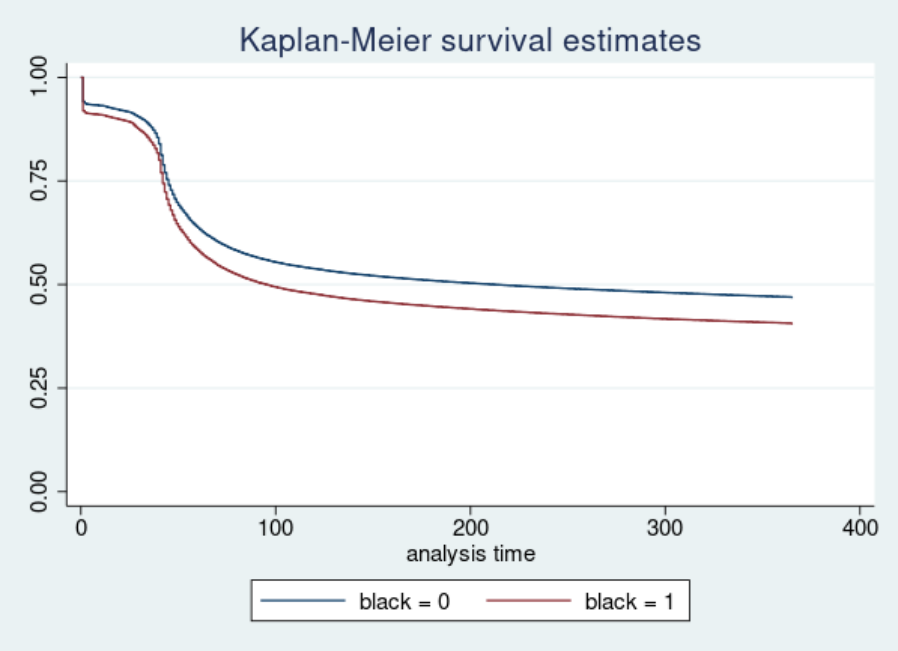


Figure 6. Delivery in State with ≥15% Population in Poverty Kaplan-Meier Survival Curve Estimates

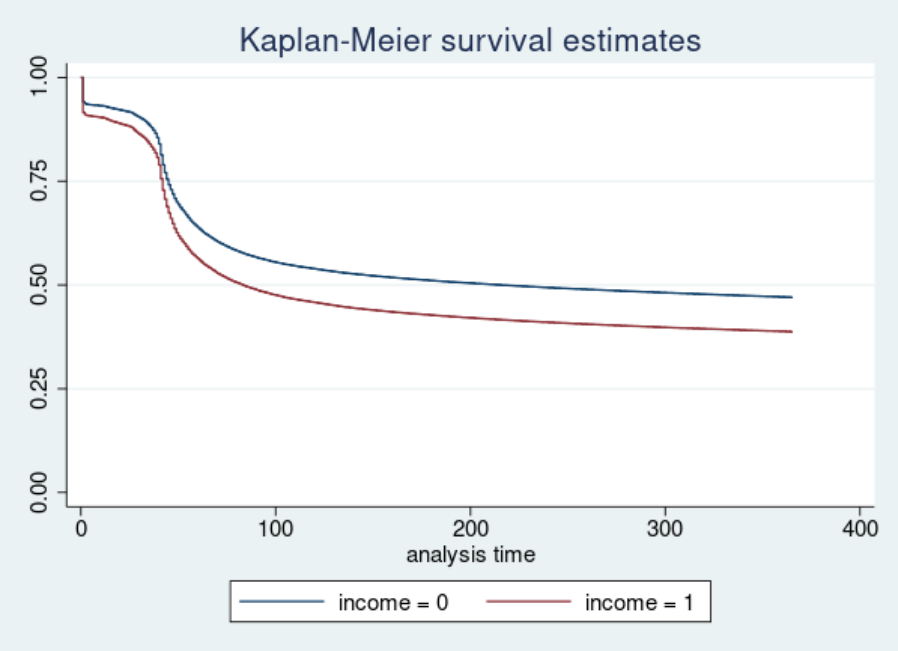


Figure 7. Delivery in State with ≥35% Women with College Degree or More Kaplan-Meier Survival Curve Estimates

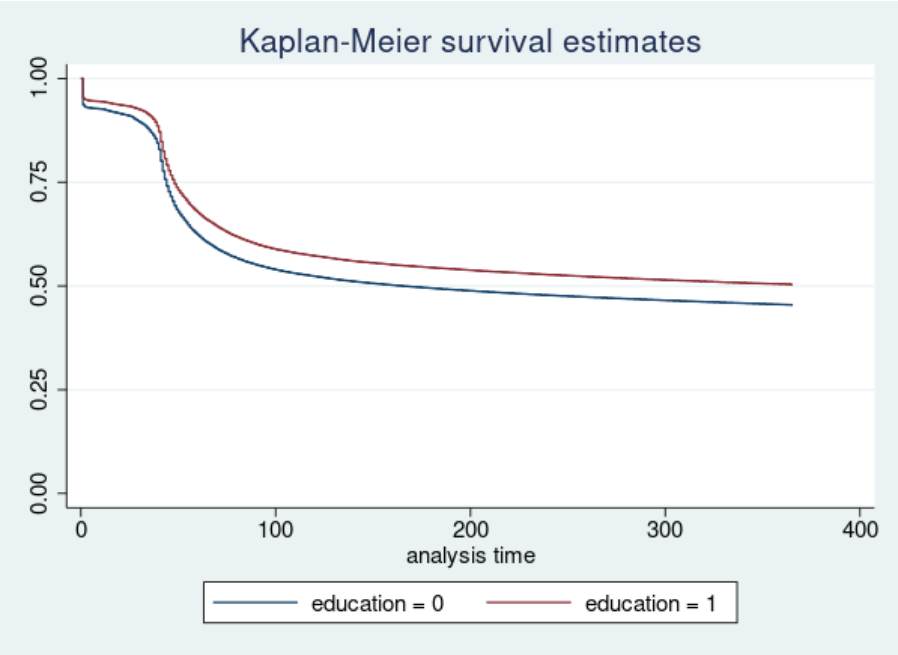


Figure 8. Delivery Mode Kaplan-Meier Survival Curve Estimates

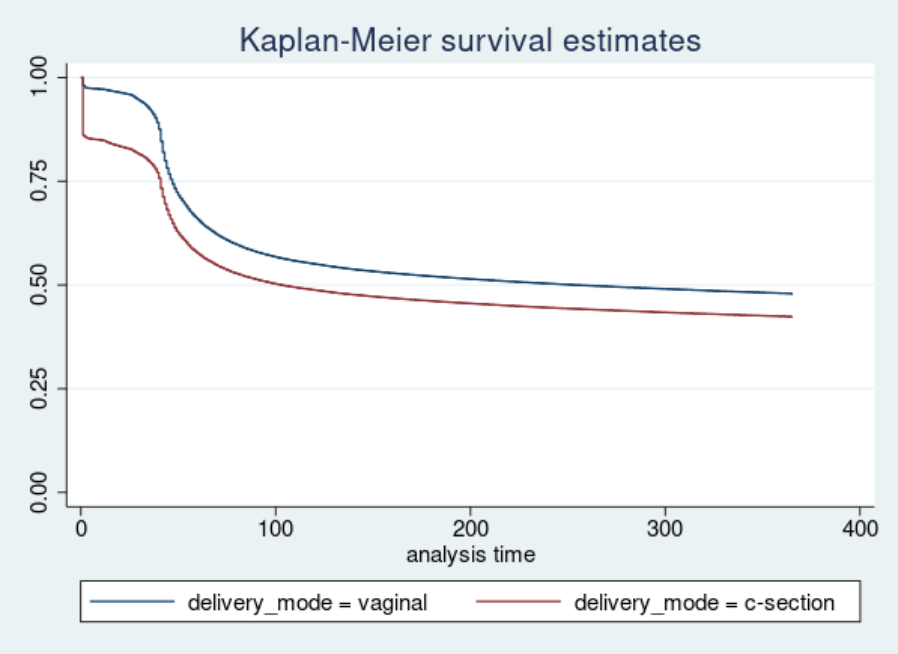


Figure 9. Insurance Plan Type Kaplan-Meier Survival Curve Estimates

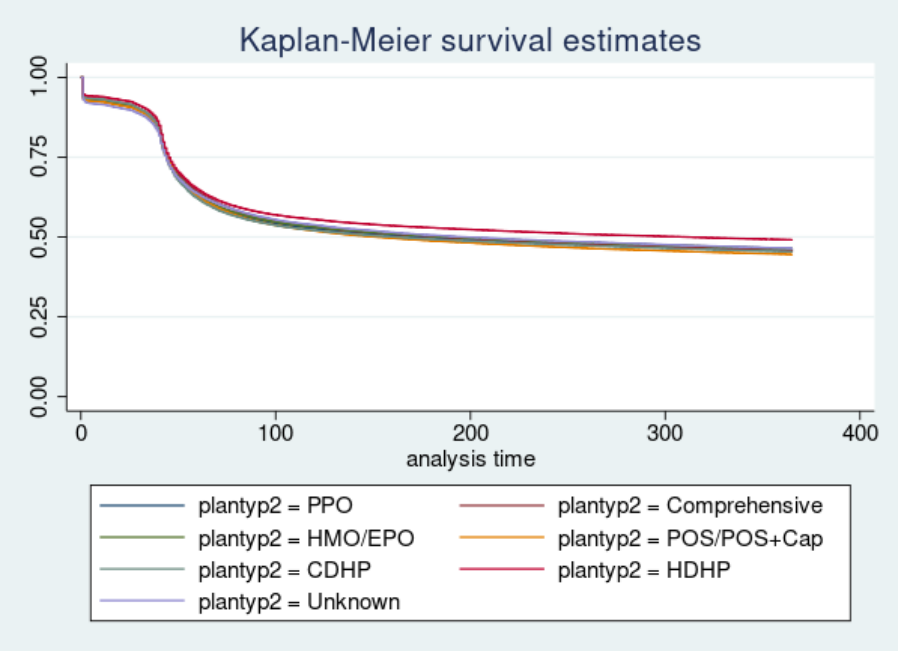


Figure 10. Year of Delivery Kaplan-Meier Survival Curve Estimates

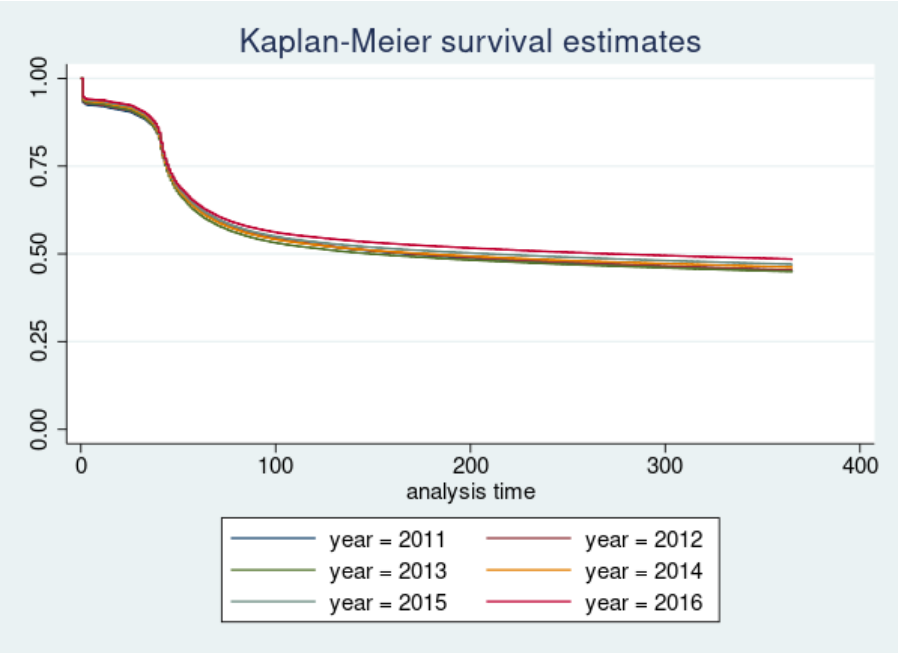


Figure 11. Any Psychiatric Diagnosis Kaplan-Meier Survival Curve Estimates

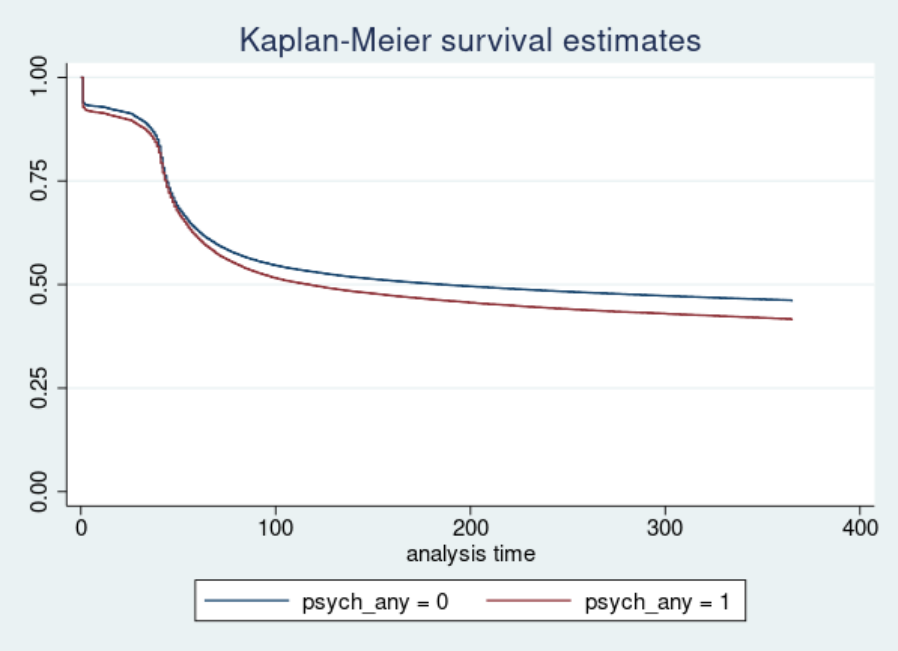


Figure 12. Non-Opioid Substance Use Disorder Kaplan-Meier Survival Curve Estimates

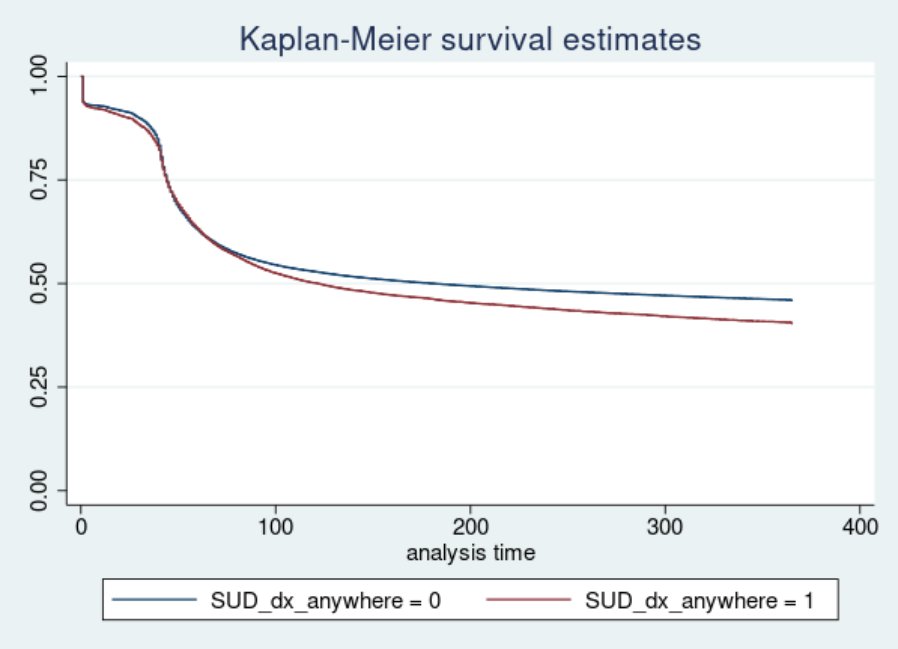


Figure 13. Autoimmune Disease Kaplan-Meier Survival Curve Estimates

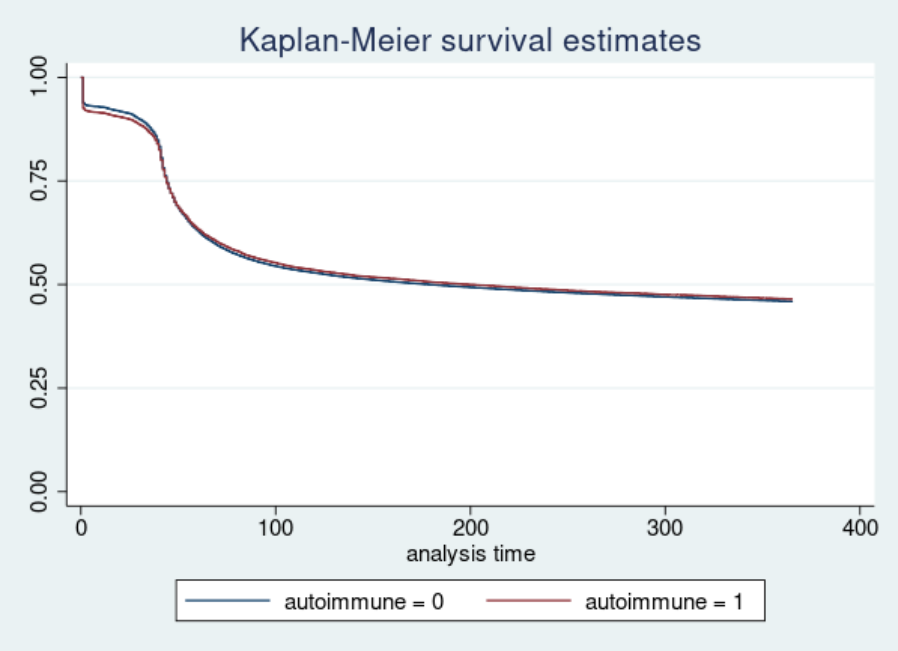


Figure 14. Diabetes Mellitus Kaplan-Meier Survival Curve Estimates

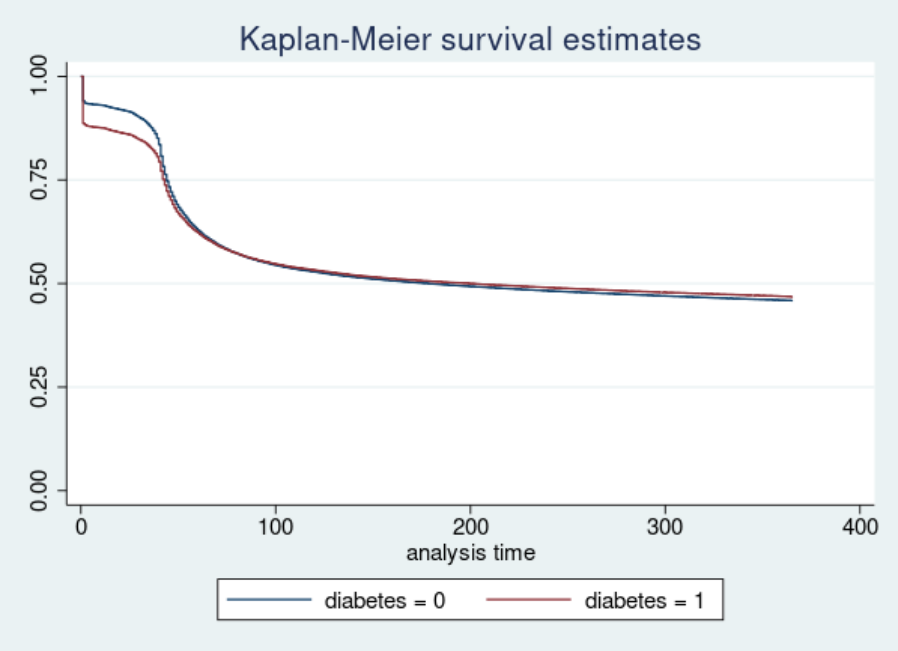


Figure 15. Gestational Diabetes Kaplan-Meier Survival Curve Estimates

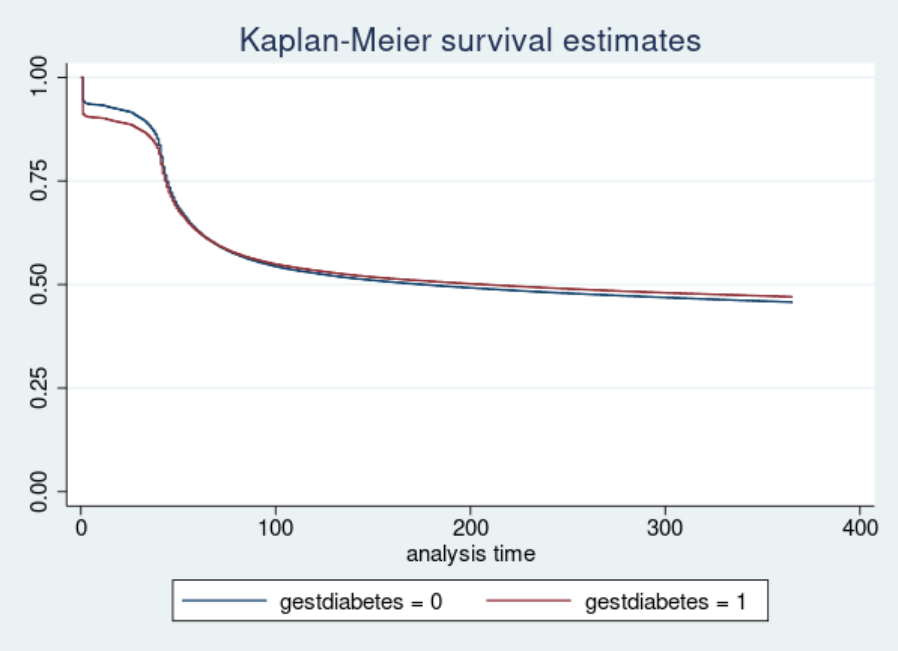


Figure 16. Chronic Hypertension Kaplan-Meier Survival Curve Estimates

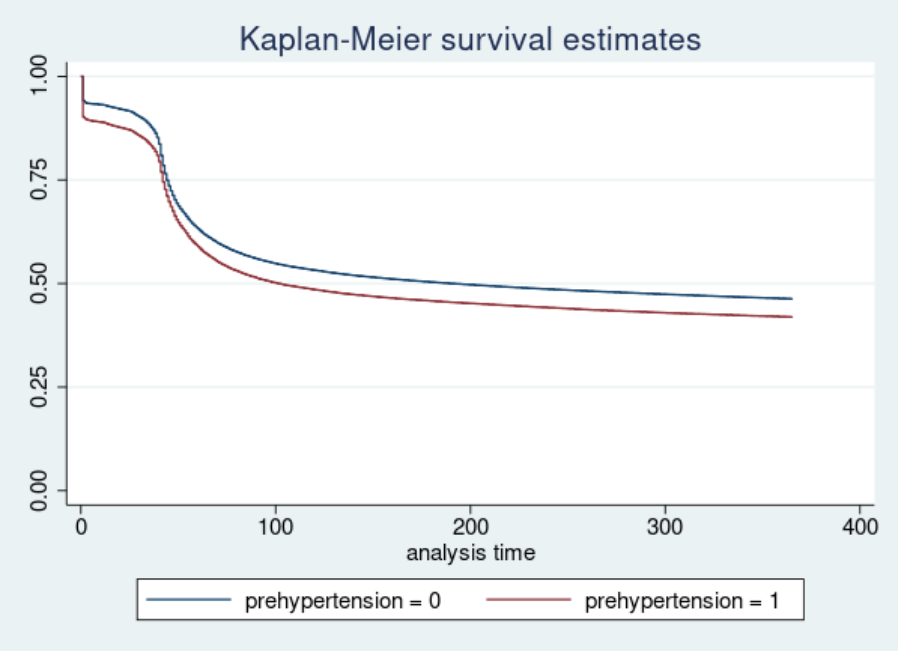


Figure 17. Gestational Hypertension Kaplan-Meier Survival Curve Estimates

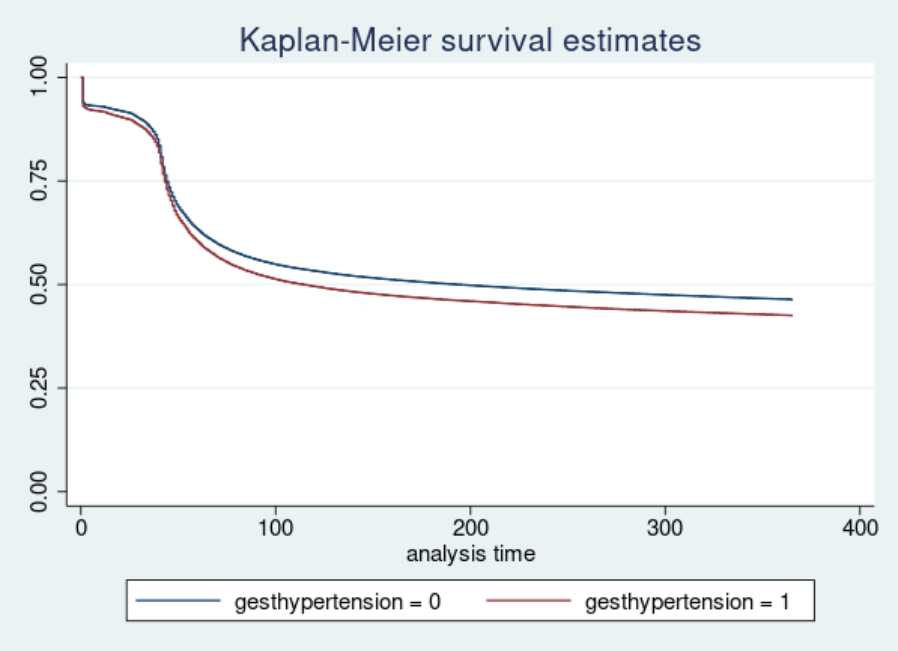


Figure 18. Asthma Kaplan-Meier Survival Curve Estimates

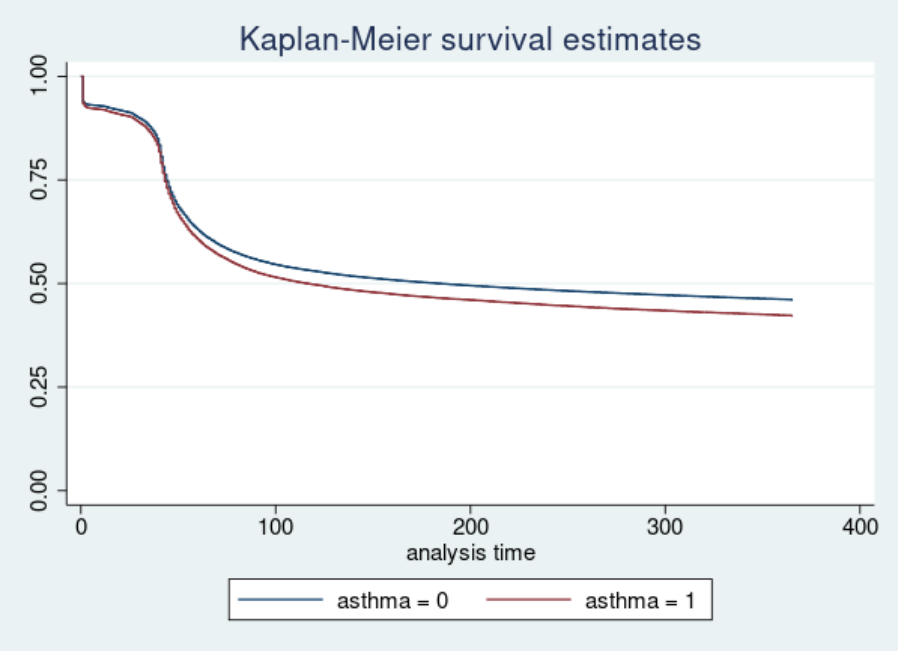


Figure 19. Pain Conditions Kaplan-Meier Survival Curve Estimates

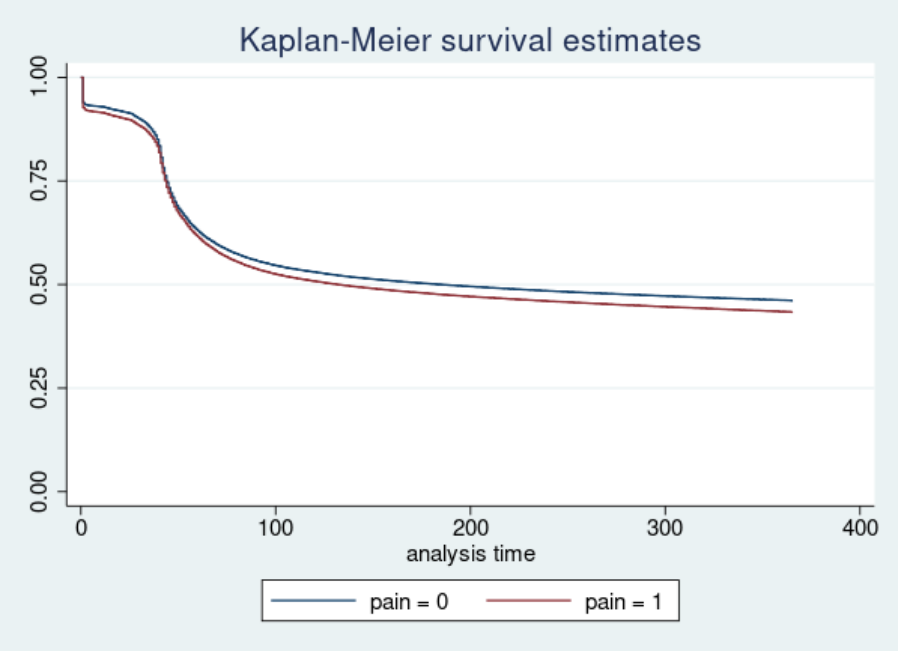


Figure 20. Hepatitis C Kaplan-Meier Survival Curve Estimates

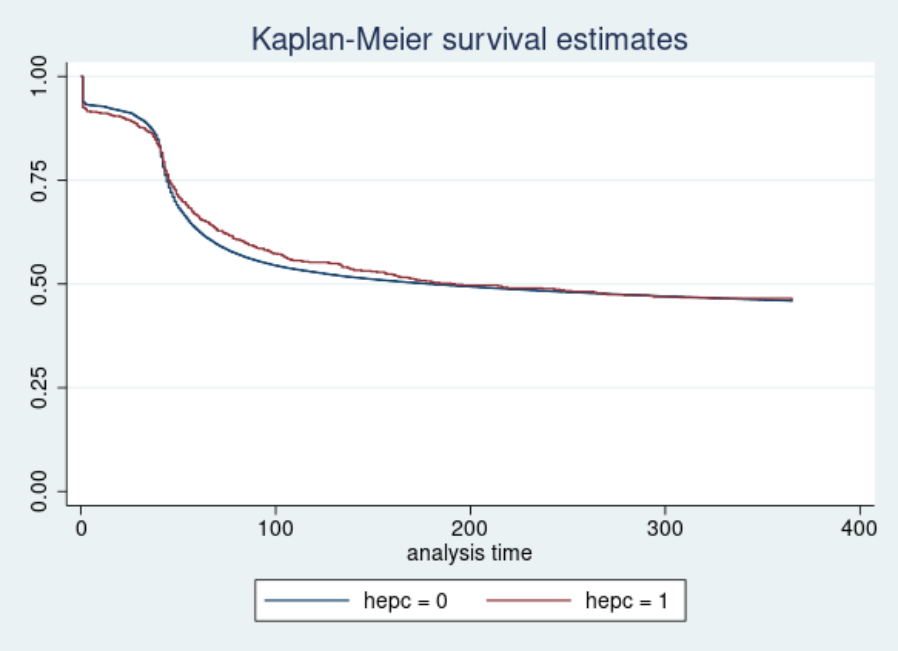


Figure 21. Any Antenatal Care Visits Kaplan-Meier Survival Curve Estimates

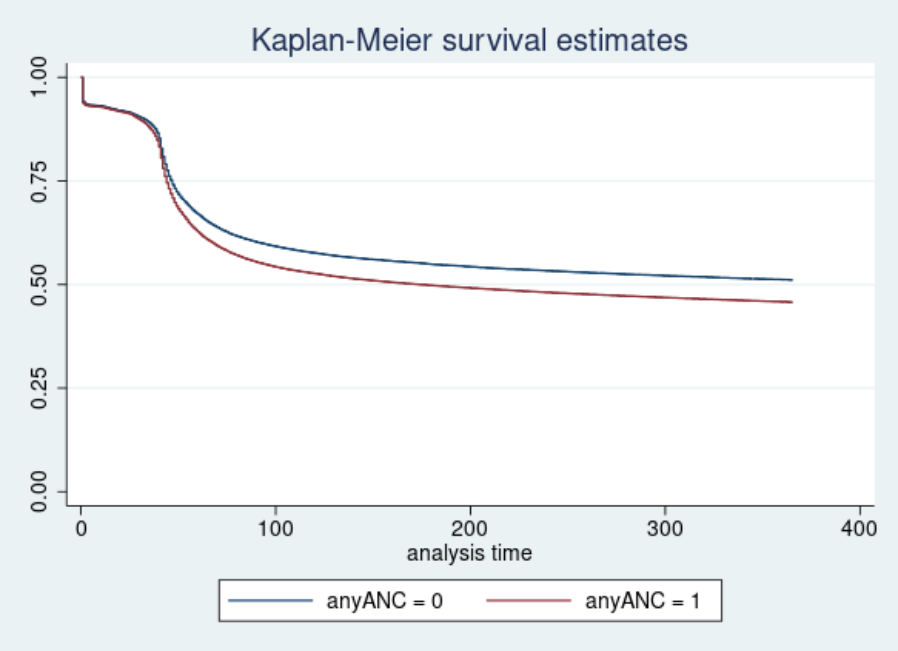


Figure 22. Opioid Use During Pregnancy Log-Log Plot

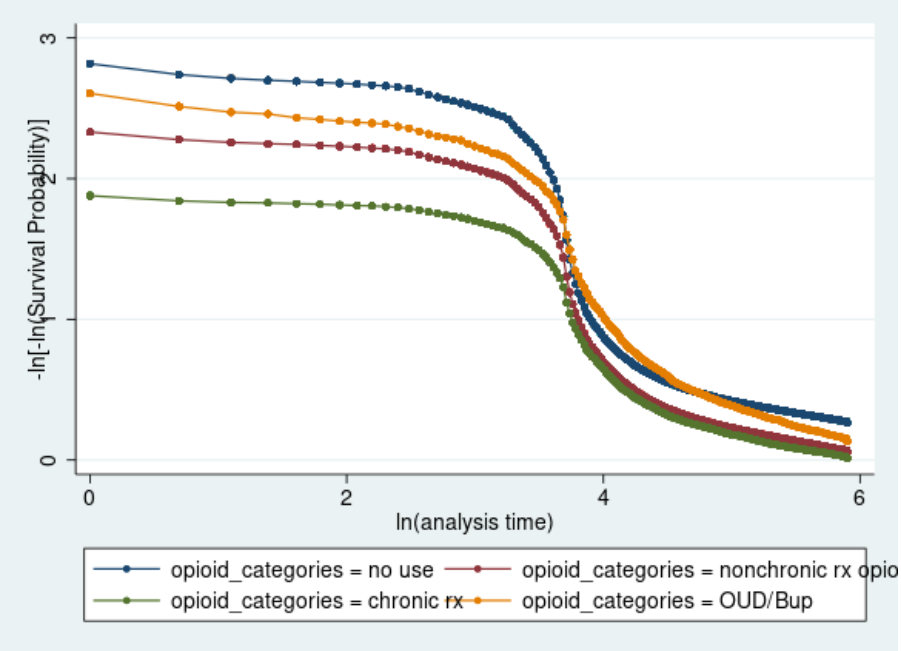


Figure 23. Maternal Age Log-Log Plot

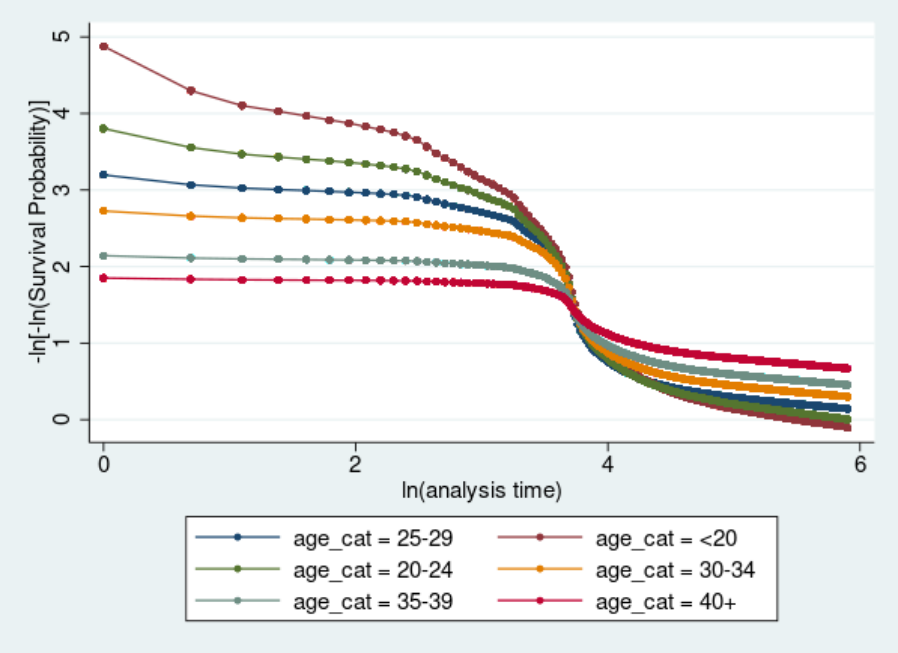


Figure 24. HRSA Region Log-Log Plot

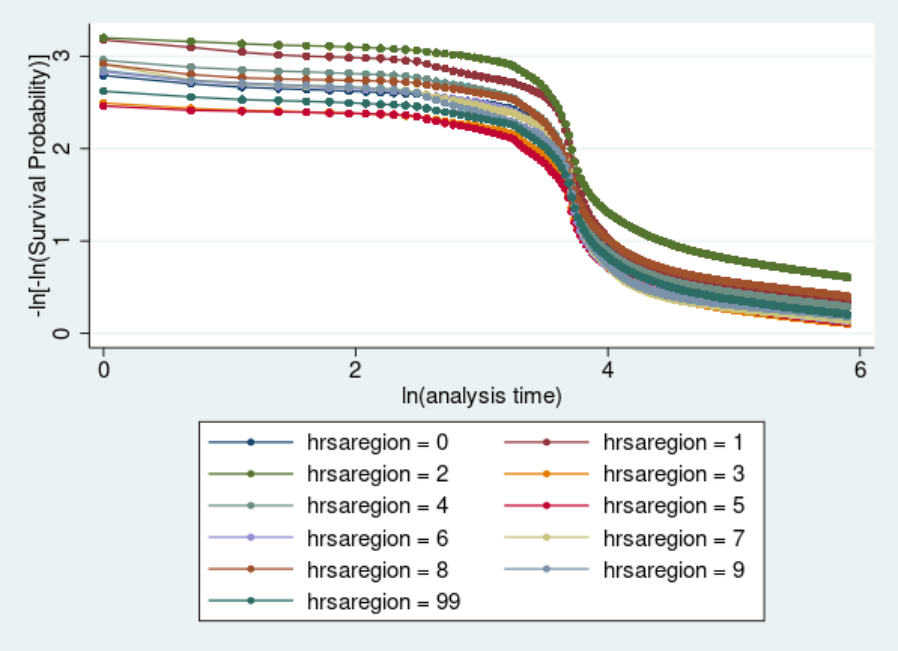


Figure 25. Delivery in State with ≥20% Hispanic Population Log-Log Plot

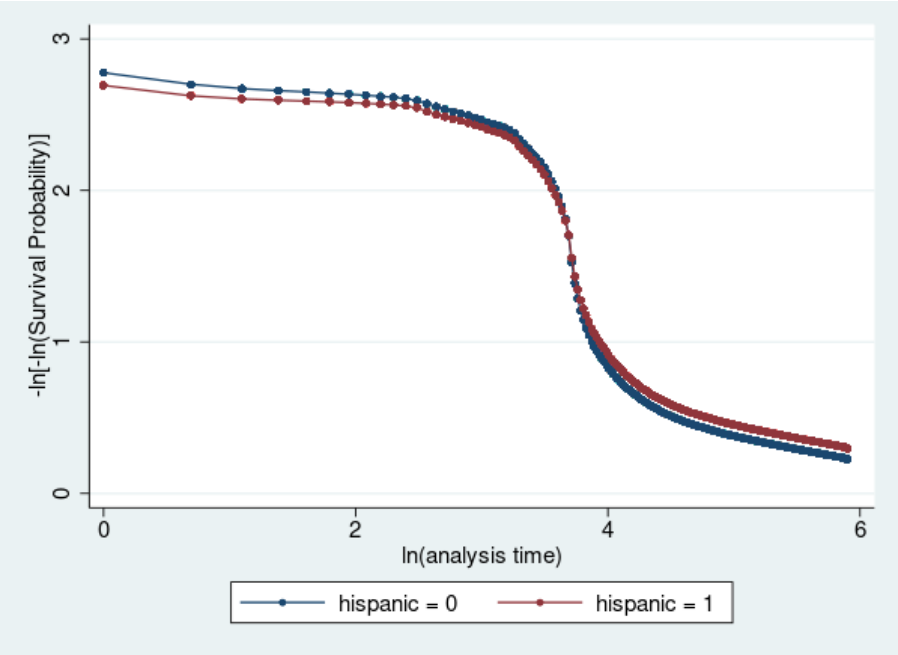


Figure 26. Delivery in State with ≥20% Black Population Log-Log Plot

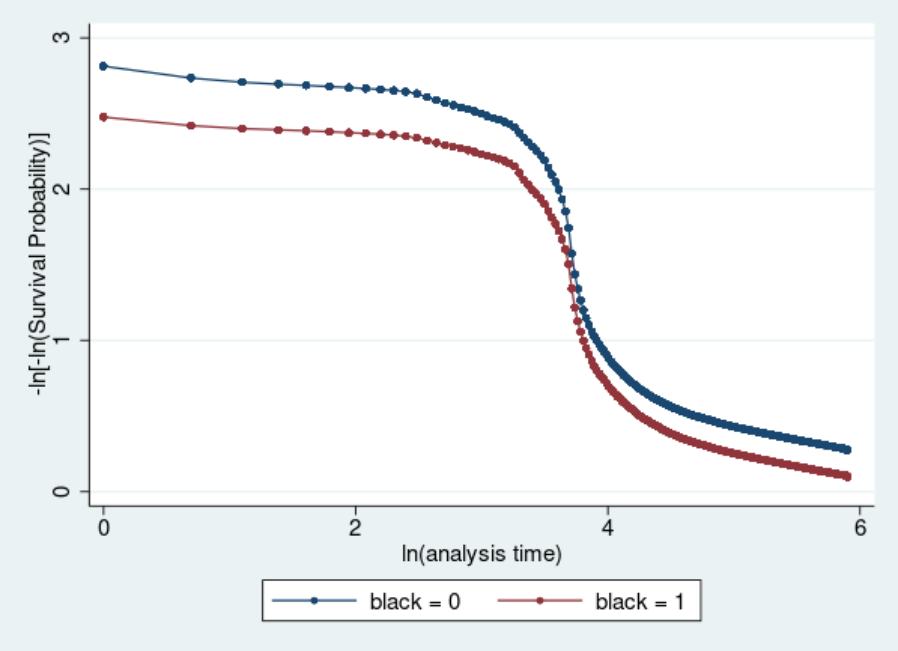


Figure 27. Delivery in State with ≥15% Population in Poverty Log-Log Plot

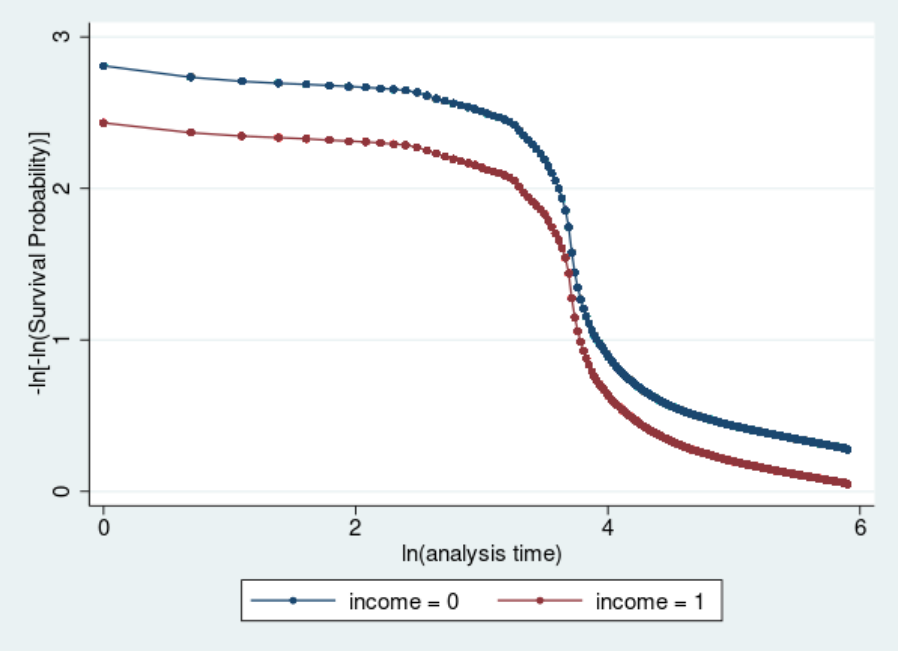


Figure 28. Delivery in State with ≥35% Women with College Degree or More Log-Log Plot

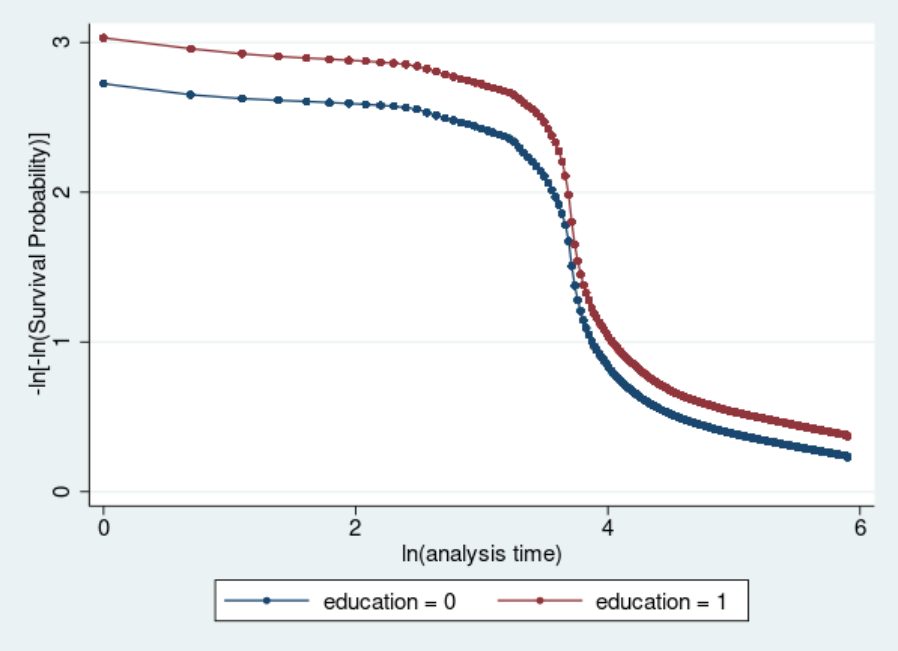


Figure 29. Delivery Mode Log-Log Plot

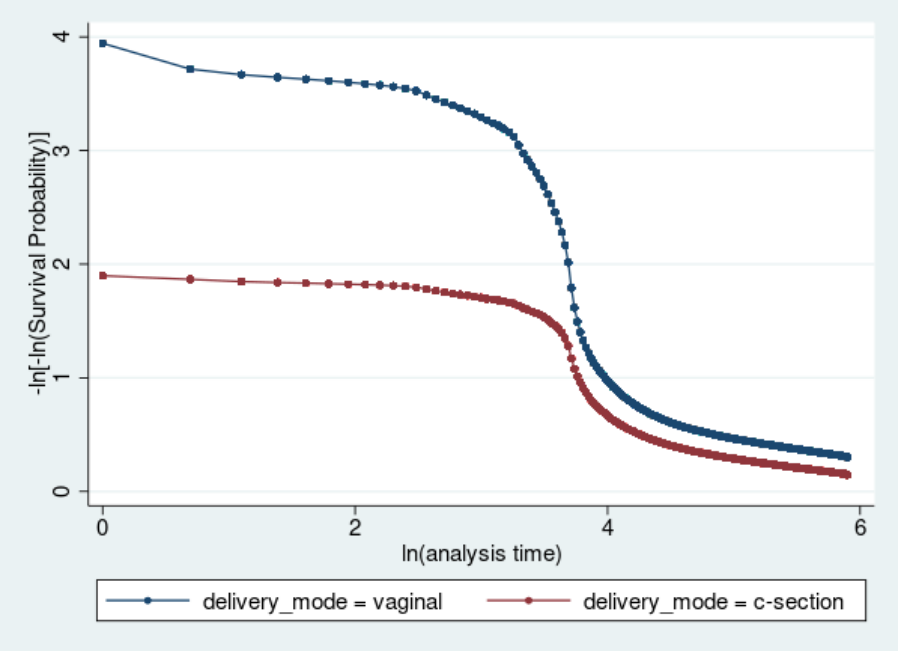


Figure 30. Insurance Plan Type Log-Log Plot

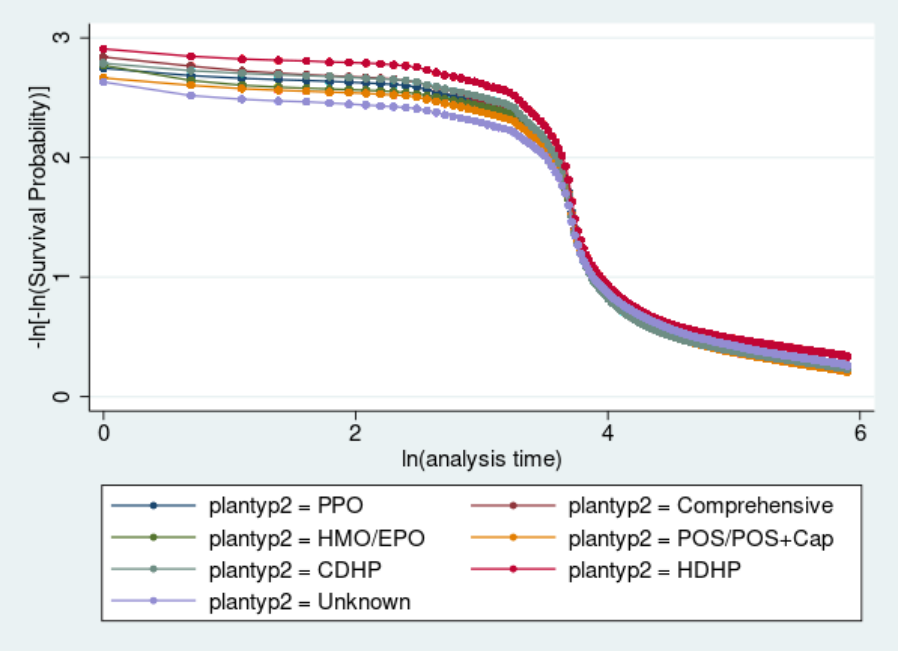


Figure 31. Year of Delivery Log-Log Plot

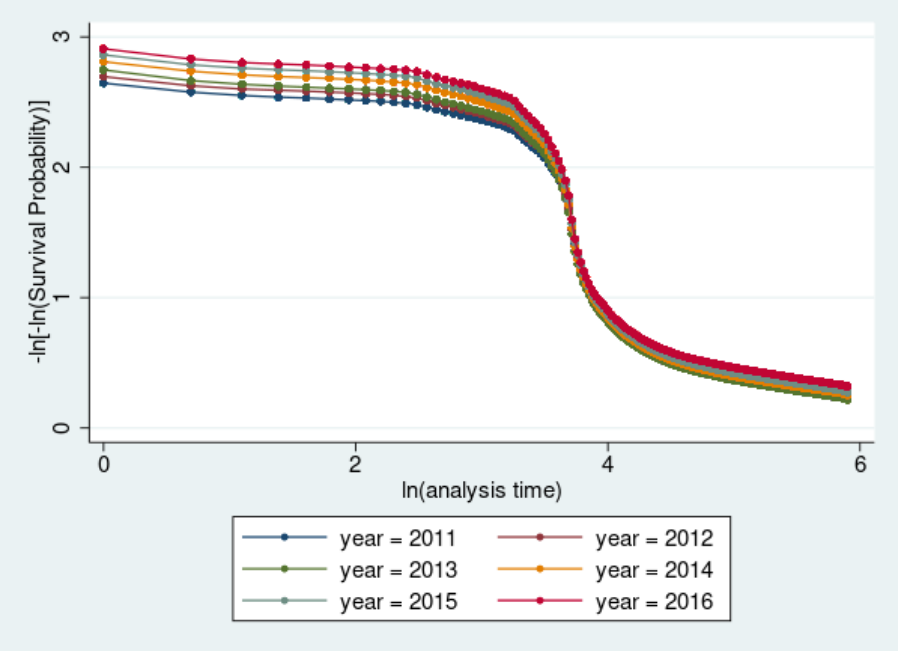


Figure 32. Psychiatric Diagnosis Log-Log Plot

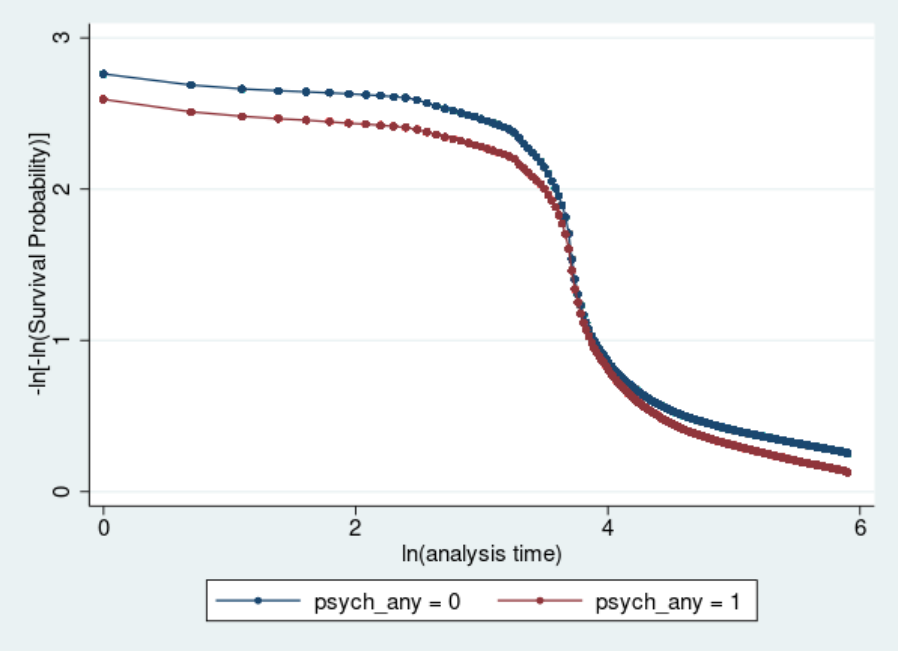


Figure 33. Non-Opioid Substance Use Disorder Log-Log Plot

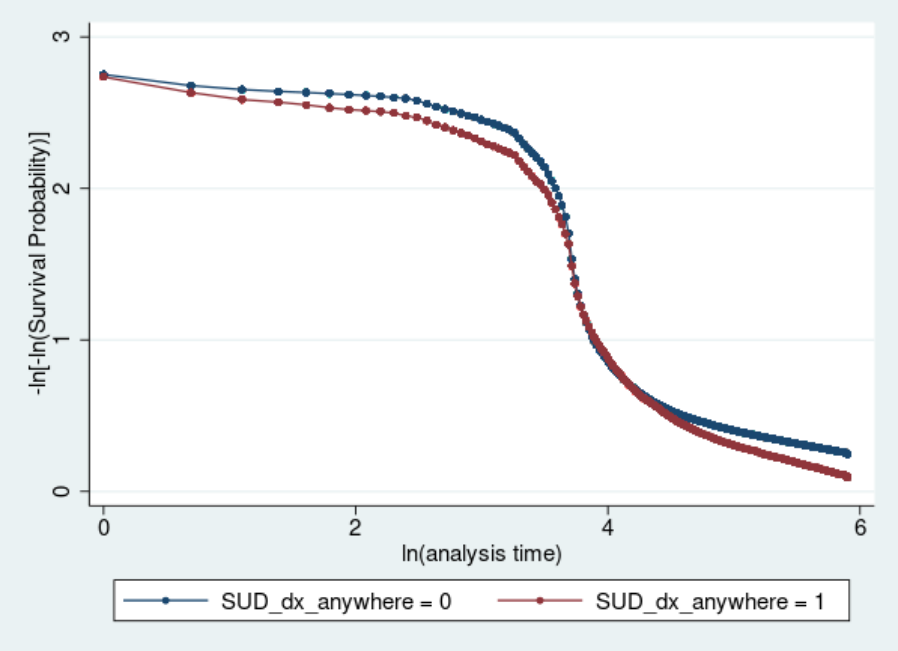


Figure 34. Autoimmune Disease Log-Log Plot

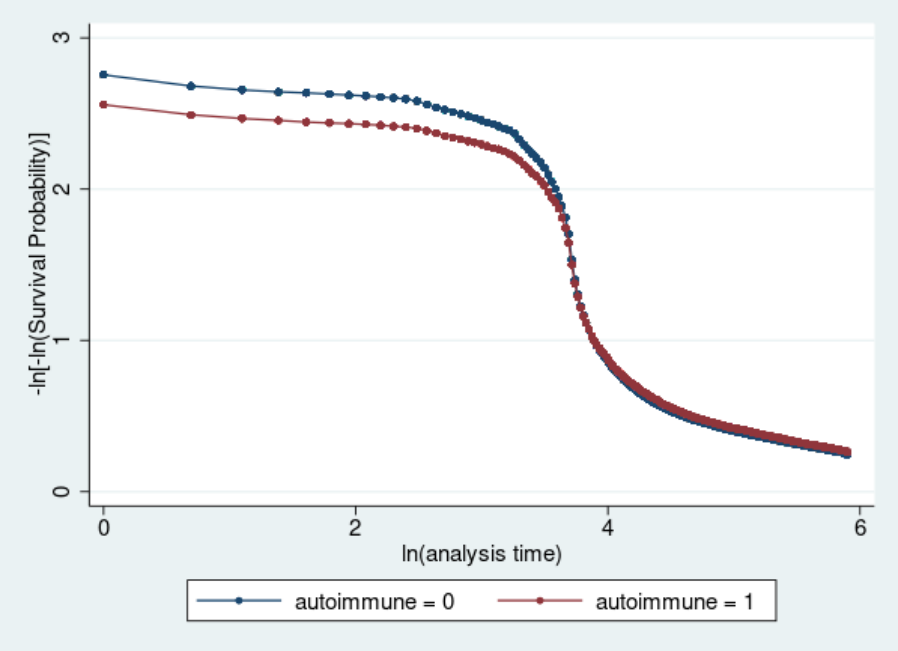


Figure 35. Diabetes Mellitus Log-Log Plot

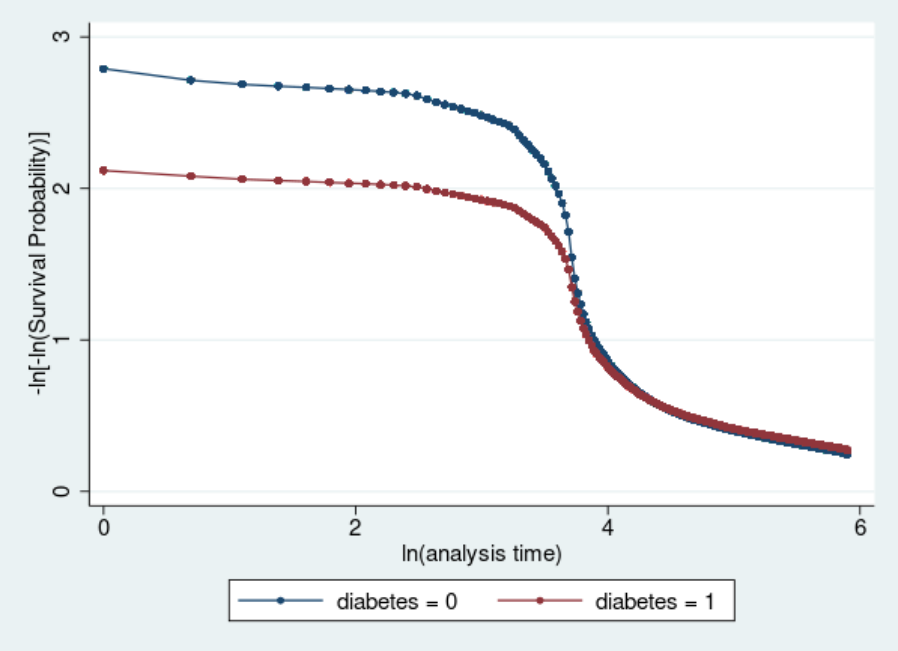


Figure 36. Gestational Diabetes Log-Log Plot

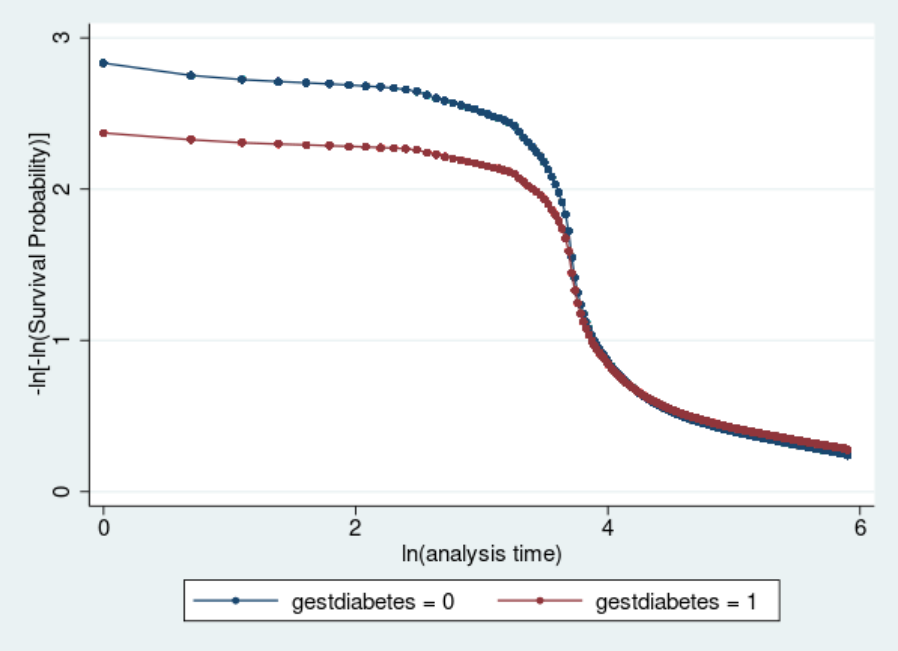


Figure 37. Chronic Hypertension Log-Log Plot

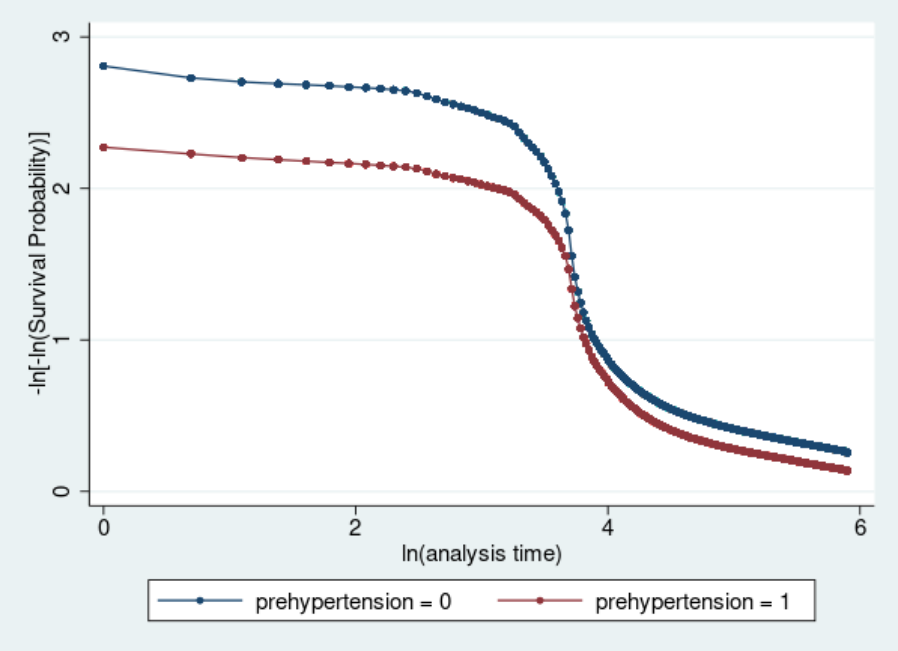


Figure 38. Gestational Hypertension Log-Log Plot

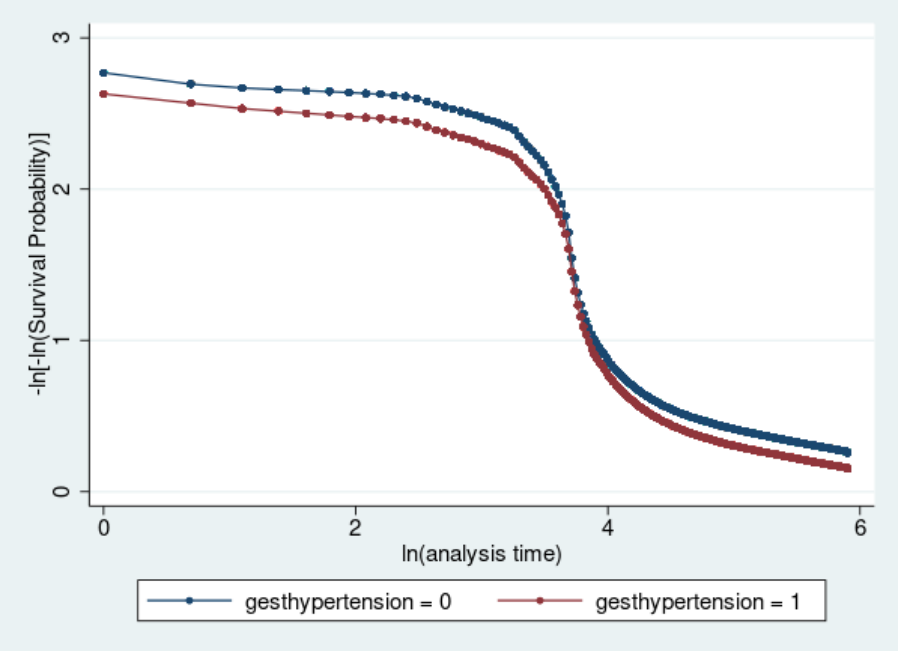


Figure 39. Asthma Log-Log Plot

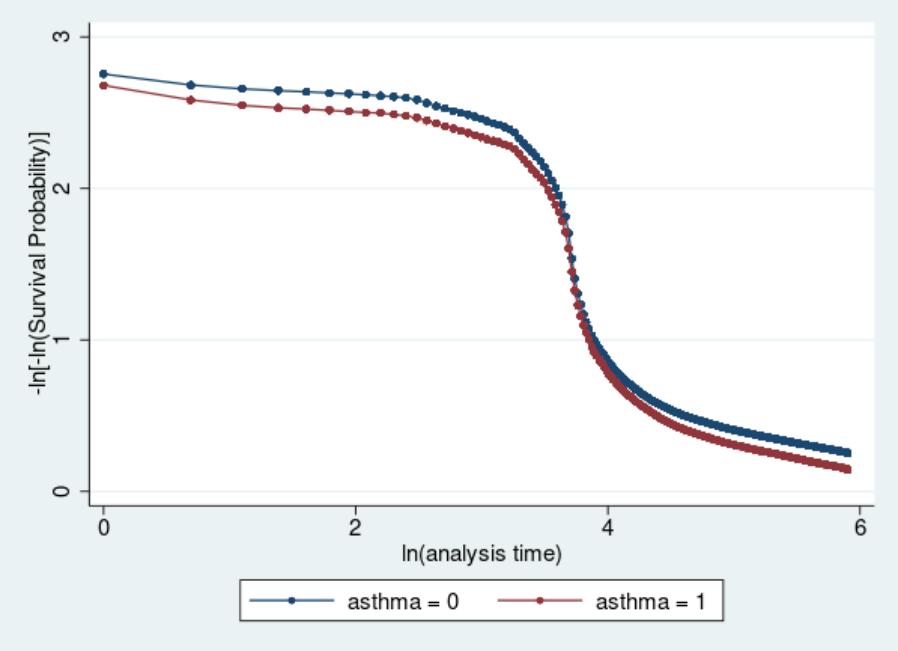


Figure 40. Pain Conditions Log-Log Plot

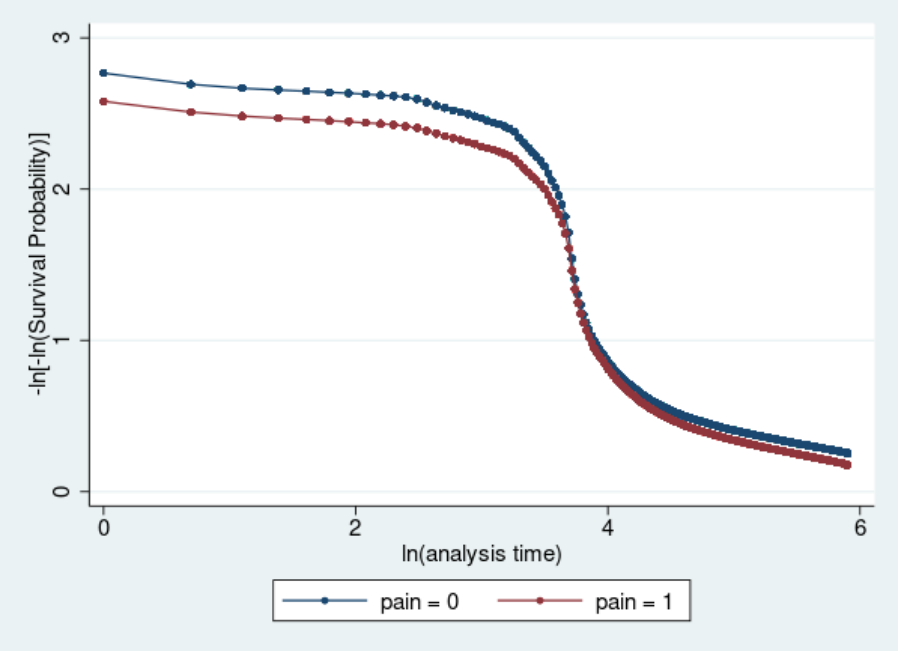


Figure 41. Hepatitis C Log-Log Plot

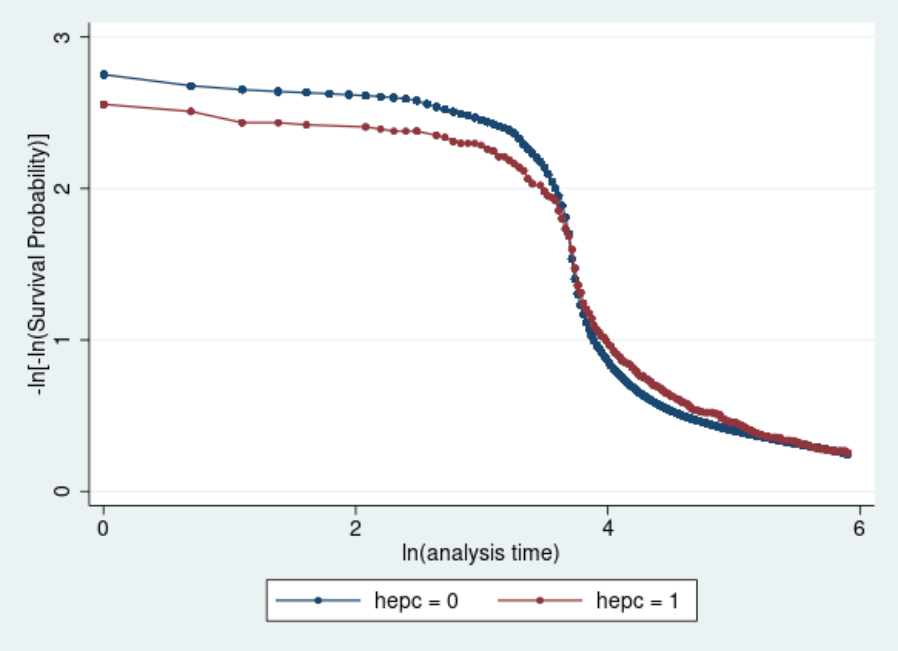
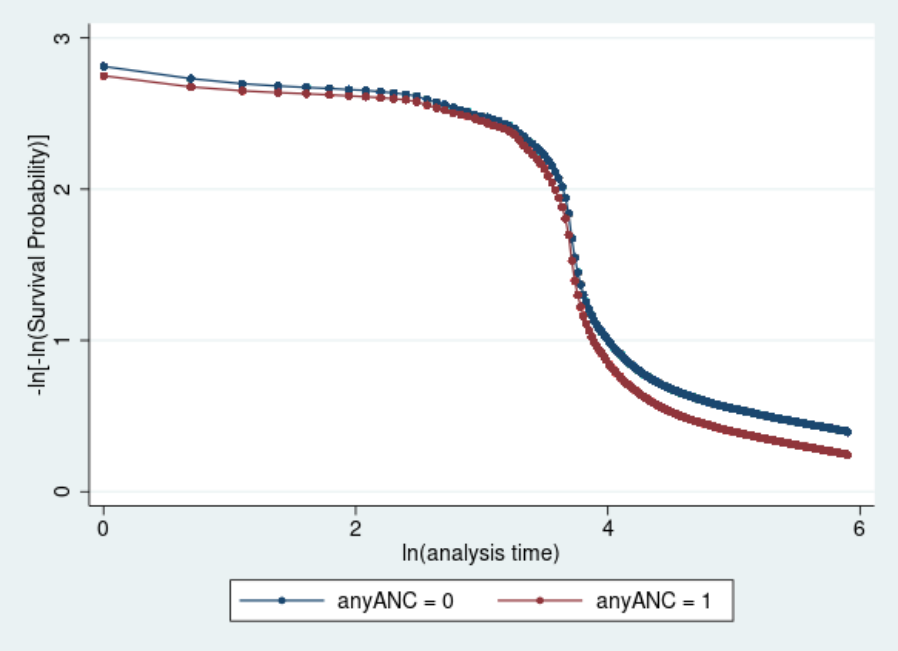


Figure 42. Any Antenatal Care Visits Log-Log Plot



Curriculum Vitae

Leah G. Horton, MSPH

12 Cranston Rd.
Winchester MA 01890
(610) 716-0281 | lhorton15@gmail.com

OBJECTIVE

Lead innovative research and develop evidence-based programs in the field of maternal and reproductive health to address reproductive health disparities among socially disadvantaged groups in the U.S.

EDUCATION

Johns Hopkins Bloomberg School of Public Health Baltimore, MD
PhD Student, Population, Family and Reproductive Health Department
- Focal Area: Maternal, Fetal and Perinatal Health

MSPH, Reproductive, Perinatal, and Women's Health May 2015
- Certificate: Maternal and Child Health
- GPA: 3.9
- Maternal and Child Health Training Grant recipient
- Thesis: *Prenatal Drug Use and the American Response: A Policy Analysis*
  - This policy analysis explored current laws and policies directed towards women who use drugs while pregnant, assessed the strengths and weaknesses of those policies, and applied evidence-based theory to identify future policy strategies.

Johns Hopkins University, Krieger School of Arts and Sciences Baltimore, MD
B.A. in Public Health Studies May 2009

FELLOWSHIPS & AWARDS

The Kann Trowbridge Fund, *PFRH, JHSPH* March, 2019
Maternal and Child Health Epidemiology Fellow, *Maternal and Child Health Bureau* Sept, 2018
The Kann Trowbridge Fund, *Population and Family Department, JHSPH* March, 2018
The John and Alice Chenoweth-Pate Fellowship, *PFRH, JHSPH* March, 2017
Reproductive Epidemiology Fellowship, *Centers for Disease Control and Prevention* July 2015
Special Achievement Award, *U.S. Department of Justice* December 2010
Graduated with Honors, *Johns Hopkins University* May 2009

PUBLICATIONS

Horton LG, Folger SG, Berry-Bibee E, Jatlaoui TC, Tepper NK, Curtis KM. *"Research gaps from evidence-based contraception guidance: the U.S. Medical Eligibility Criteria for Contraceptive Use 2016, and the U.S. Selected Practice Recommendations for Contraceptive Use, 2016".* Contraception, 2016 Dec;94(6):582-589.

Horton LG, Simmons KB, Curtis KM. *"Combined hormonal contraceptive use among obese women and risk for cardiovascular events: a systematic review".* Contraception, 2016 Dec;94(6):590-604.

Holliday CN, **Horton L**, Decker MR, Strobino, D, Thorpe RJ. Racial/Ethnic differences in unintended pregnancy risk: A multi-level examination of women's health risk factors. [Poster Presentation]. American Public Health Association Conference, San Diego, CA, November 2018.

Curtis KM, Jatlaoui TC, Tepper NK, Zapata LB, **Horton LG**, Jamieson DJ, Whiteman MK. *"U.S. Selected Practice Recommendations for Contraceptive Use, 2016".* MMWR Recomm Report, 2016;64(4):1-66.

Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, **Horton LG**, Zapata LB, Simmons KB, Pagano HP, Jamieson DJ, Whiteman MK. *"U.S. Medical Eligibility Criteria for Contraceptive Use, 2016".* MMWR Recomm Report, 2016;65(3):1-103.

Ermias Y, Morgan IA, Curtis KM, Whiteman MK, **Horton LG**, Zapata LB. *"Factors Associated with Provision of Depot Medroxyprogesterone Acetate to Adolescents by U.S. Health Care Providers"*. Contraception, 2019.

Mosher W, Bloom T, Hughes R, **Horton L**, Mojtabai R, Alhusen JL. "*Disparities in receipt of family planning services by disability status: new estimates from the National Survey of Family Growth.*" Disability Health Journal, 2017 Jul;10(3):394-399.

Mosher W, Bloom T, Hughes R, **Horton L**, Mojtabai R, Alhusen JL. "*Contraceptive use by disability status: new national estimates from the National Survey of Family Growth.*" Contraception, 2018 Jun;97(6):552-558.

Assaf, Shireen, **Leah Horton**, Marta Bornstein, and Thomas Pullum. 2017. *Levels and Trends of Maternal and Child Health Indicators in 11 Middle East and North African Countries*. DHS Comparative Report No. 46. Rockville, Maryland, USA: ICF.

PRESENTATIONS

"The Opioid Epidemic and Women" March, 2020

- Lecture given in graduate-level course "Women's Health" (380.666.01) taught by Dr. Michelle Decker at Johns Hopkins School of Public Health

"Substance Use and Women" May, 2019

- Lecture given in graduate-level course "Women's Health Policy" (380.667.01) taught by Dr. Charvonne Holliday at Johns Hopkins School of Public Health

"Obesity and Combined Hormonal Contraceptives." August, 2015

- Presentation given at the CDC in Atlanta, GA for the U.S. Medical Eligibility Criteria for Contraceptive Use/Special Practice Recommendations for Contraceptive Use Update meeting

PROFESSIONAL EXPERIENCE

U.S.CDC, Division of Reproductive Health Atlanta, GA

ASPPH/CDC Reproductive Epidemiology Fellow July 2015-July 2016

- Member of the Fertility Epidemiology Studies Team responsible for the creation and dissemination of the U.S. Medical Eligibility Criteria for Contraceptive Use (U.S. MEC) and the Special Practice Recommendations for Contraceptive Use (U.S. SPR)
  - These guidelines help clinicians and healthcare providers across the country prescribe contraception to women with medical conditions and certain personal characteristics that may make some forms of contraception unsafe or sub-optimal.
- Responsible for updating the U.S. MEC and U.S. SPR for publication in the summer of 2016: editing documents for internal and external consistency; managing the references; updating the recommendations
- Lead the U.S. MEC recommendation update for "Safety of Combined Hormonal Contraceptive Use among Women with Obesity" which resulted in the publication of a systematic review
- Analyzed complex survey data from a CDC-lead complex survey examining the attitudes and practices of family planning providers across the U.S.
  - Using multivariable logistic regression to examine the associations between practitioner attitudes and practices and the provision of DMPA to adolescents; manuscript pending
- Worked closely with World Health Organization counterparts on the international versions of the SPR and MEC
- Maintained the web-based Continuous Identification of Research Evidence (CIRE) system tracking contraception and family planning peer reviewed literature

Jhpiego Baltimore, MD/Washington D.C.

Monitoring, Evaluation & Research Intern January 2014- July 2015

- Support a mixed methods study concerning the integration of postpartum family planning services in Kenya and India
  - Organize and design quantitative mobile data collection survey for this study using a tablet-based platform
- Lead two extensive literature reviews pertaining to neonatal and maternal health outcomes and maternal nutrition
- Conduct an internal assessment of the organization and data collection practices to determine the value of performing an impact analysis
- Design and develop the 2014 fiscal year-end review presentation encompassing all Jhpiego activities

Planned Parenthood Southeastern Pennsylvania Philadelphia, PA
Research Coordinator Intern September-December 2014

- Recruit, consent, and enroll subjects for current clinical studies involving reproductive health issues
- Provide support for research studies, including maintaining enrollment logs, managing institutional review boards (IRBs) and case report forms, and handling specimens in laboratory
- Assist in preparing documents for regulatory agencies including Planned Parenthood Federation of American, multiple IRBs, contract research organizations, and the Food and Drug Administration

Advisory Board Company Washington, DC
Healthcare Senior Associate Nov 2011-August 2013

- A member of the Hospital Operations and Strategy Consulting group providing consulting services for hospitals including operational, labor, and strategic assessments and implementation
- Project managed multiple engagements at client hospitals located across the country, ranging in size, technological integration, and specialties
- Each engagement includes extensive data collection and analysis across all facets of hospital operations
  - Typical data analysis includes operating room utilization, bed capacity and utilization, cost-per-case (both surgical and medical), and patient transfer rates across hospital units
- Comprehensive document creation and presentation to executives showcasing opportunities for hospital process improvement
- Primary duties were data driven but also included relationship management with client, extensive on-site time, and analytical as well as qualitative assessment of hospital methods compared to best practice standards

United States Department of Justice, Criminal Division, Fraud Section Washington, DC
Honors Paralegal Program – Litigation Paralegal Specialist Sept 2009-Nov 2011

- Lead Paralegal on a 24 defendant, $205 million corporate healthcare fraud case (*US v. Lawrence Duran et al)*
- Draft indictment packets; pleadings, motions, exhibit and witness lists, discovery correspondence

RESEARCH AND TEACHING EXPERIENCE

Risk Factor for Adverse Birth Outcomes in Nepal October 2018-Present

- Lead by Drs. Joanne Katz, Luke Mullany, Bob Black, Scott Zeger, and Andreea Creanga
- This project seeks to identify modifiable risk factors for stillbirth, preterm and small-for-gestational age birth, and neonatal mortality using longitudinal data from four randomized controlled trials in rural Nepal
- Responsibilities include devising analysis plans, merging and managing complex data sets, and working with team members to align the data with known risk factors for adverse birth outcomes

REGIONS Study: Reproductive Experiences Given the Influence of One's Neighborhood
May 2018-Dec 2019

- Lead by Dr. Charvonne Holliday, this work will explore how place-based factors influence sexual and reproductive outcomes, particularly among marginalized groups
- Leading the descriptive and statistical analyses for multiple portions of this project using several sources of data including PRAMS, survey data, and Los Angeles Mommy and Baby study data
- Using geospatial analysis techniques to identify the relationship between community-levels factors and sexual and reproductive health outcomes
- Contributing to the writing and submission of current and future manuscripts derived from the REGION study

R-21 Grant: Unintended Pregnancy among Women with Disabilities Sept 2016-May 2018

- Lead by Dr. William Mosher, our team is examining the reproductive health status of women with disabilities in the United States using data from the National Survey on Family Growth
- This work is among the first of its kind to use a nationally representative dataset to examine sexual, reproductive, and fertility outcomes among women with disabilities in the U.S.
- Several publications have resulted from this work, with two other manuscripts currently in process
- Performing the descriptive and statistical analysis for several manuscripts including those exploring access and use of family planning services, contraceptive use, and screening for cervical cancer among women with and without disabilities

Strengthening the Evidence June 2017-January 2018

- Lead by Dr. Cynthia Minkovitz and Dr. Donna Strobino, this project examines the evidence associated with 15 National Performance Measures designed to improve maternal and child health in the United States
- Undertaking a systematic review of the interventions and grey literature associated with reducing child exposure to second-hand smoke

Demographic and Health Surveys Program February-September 2017

- Project documenting recent trends in maternal and child health outcomes in 11 Middle Eastern and North African countries using survey data, recent scientific literature, and grey literature
- Responsible for conducting literature reviews for all 11 countries and writing reports for each, documenting trends over the past decade pertaining to maternal, child, and infant health, health infrastructure, and special populations such as refugees

Teaching Assistant Experience September 2013-December 2019

- Undergraduate class: "Population, Health, and Development" taught by Professor Stan Becker, Head Teaching Assistant
- Graduate class: "Women's Health Policy" taught by Professor Donna Strobino & Assistant Professor Charvonne Holliday
- Graduate class: "Fundamentals of Program Evaluation" taught by Professor Kristin Mmari
- Graduate class: "Maternal and Child Health Legislation and Programs" taught by Professors Cynthia Minkovitz and Sara Riese

- Graduate class: “Population Dynamics” taught by Professors Henry Mosley, ME Hughes, Donna Strobino, and Li Liu
- Graduate class: “Health Survey Research Methods” taught by Professor Susan Sherman
- Graduate class: “Clinical Issues in Maternal and Newborn Health” taught by Professors Pamela Donohue and Donna Strobino
- Graduate class: “Critiquing the Research Literature in Maternal, Neonatal, and Reproductive Health” taught by Professor Donna Strobino
- Graduate class: “Life Course Perspectives on Health” taught by Professors ME Hughes and Cynthia Minkovitz

Software Knowledge

- Advanced knowledge of Excel, Word, Powerpoint, Stata16, EndNote